Ministry of Health of the Republic of Belarus
Educational Institution
“Gomel State Medical University”

Department of Pathological Anatomy

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METHODICAL GUIDELINES

for conducting a practical class
in the academic discipline “Pathological Anatomy”
for students
of the 3rd year, Faculty of International Students (instruction in English),
enrolled in the specialty
7-07-0911-01 “General Medicine”

Topic: “Tumours. Malignant tumors by anatomical location”

Duration: 3 hours

Approved at the meeting of the Department of Pathological Anatomy
(Minutes No. 1 dated 30.08.2025)

2025

EDUCATIONAL AND INSTRUCTIONAL GOALS, OBJECTIVES, AND MOTIVATION FOR MASTERING THE TOPIC

Educational Goal:

- To study the epidemiology, etiology, pathogenesis, morphology, clinical features, and prognosis of the most common malignant tumours organized by anatomical location. To analyze carcinomas of the lung (squamous cell carcinoma, adenocarcinoma, small cell carcinoma, large cell carcinoma), breast (invasive ductal carcinoma, invasive lobular carcinoma, special subtypes), colorectum (adenocarcinoma, mucinous carcinoma, signet-ring cell carcinoma), stomach (intestinal and diffuse types according to Lauren classification), prostate (acinar adenocarcinoma, ductal adenocarcinoma), cervix (squamous cell carcinoma, adenocarcinoma), endometrium (endometrioid adenocarcinoma, serous carcinoma, clear cell carcinoma), ovary (high-grade serous carcinoma, mucinous carcinoma, endometrioid carcinoma, clear cell carcinoma, germ cell tumours, sex cord-stromal tumours), kidney (clear cell renal cell carcinoma, papillary renal cell carcinoma, chromophobe renal cell carcinoma), bladder (urothelial carcinoma, squamous cell carcinoma, adenocarcinoma), thyroid (papillary carcinoma, follicular carcinoma, medullary carcinoma, anaplastic carcinoma), liver (hepatocellular carcinoma, cholangiocarcinoma), and pancreas (ductal adenocarcinoma, neuroendocrine tumours). To discuss the role of environmental factors, genetic predisposition, and precursor lesions for each location. To emphasize the importance of histological grading, staging, and molecular biomarkers (e.g., EGFR, ALK, ROS1 in lung cancer; HER2, ER, PR, Ki-67 in breast cancer; KRAS, NRAS, BRAF, MSI in colorectal cancer; PSA in prostate cancer; HPV status in cervical cancer; BRAF, TERT, RAS in thyroid cancer) for prognosis and targeted therapy.

Instructional Goal:

- Within the framework of the educational process for this academic discipline, the student must acquire not only theoretical knowledge, practical skills and abilities in the specialty but also develop their personal potential. They should cultivate qualities of responsibility and patriotism, be prepared to actively participate in the economic, socio-cultural, and public life of the country, recognize the social significance of their future professional activity, understand the norms of medical ethics and deontology, and learn to observe academic and labor discipline. In the course of studying the educational material, students should realize the importance of maintaining a healthy lifestyle and, as an example in the future, when performing professional duties, set an example for those around them and their patients.

Objectives: Upon completion of the practical session, the student must:

***Know*:**

- The most common malignant tumours by anatomical location (lung, breast, colorectum, stomach, prostate, cervix, endometrium, ovary, kidney, bladder, thyroid, liver, pancreas);

- The etiology and risk factors for each tumour type;
- The macroscopic and microscopic morphological features of each common malignant tumour;
- The prognostic factors and typical clinical behaviour (metastatic patterns) for each tumour;
- The molecular biomarkers used for diagnosis, prognosis, and targeted therapy;
- The principles of screening and early detection for common cancers.

Be able to:

- Identify the histological type of a malignant tumour based on its anatomical location and microscopic appearance;
- Diagnose pathological processes and diseases based on the description of macroscopic and microscopic changes in organs and tissues of the body;
- Correlate tumour morphology with clinical presentation and prognosis;
- Recognize precursor lesions (e.g., adenomatous polyps in colon, cervical intraepithelial neoplasia, ductal carcinoma in situ of the breast).

Master:

- Basic techniques for working with a microscope;
- Skills in clinical-anatomical analysis;
- The fundamentals of synthetic generalization of morphological diagnostic signs of diseases and their correct interpretation in cause-and-effect relationships.

Motivation for Mastering the Topic:

Cancer is a leading cause of death worldwide, and knowledge of the specific morphological features of malignant tumours arising in different organs is fundamental to clinical practice. Each anatomical location presents unique challenges in terms of early detection, differential diagnosis, prognostic assessment, and treatment selection. Understanding the relationship between tumour histology and clinical behaviour enables physicians to provide accurate prognoses and personalized therapeutic strategies. This topic integrates knowledge from all previous tumour-related topics and applies it to real-world clinical scenarios. Mastery of this material is essential for all physicians, particularly those in oncology, surgery, gynaecology, urology, gastroenterology, pulmonology, and general practice, as well as for pathologists who provide the diagnostic foundation for patient care.

QUESTIONS

1. Lung cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

2. Esophageal cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

3. Stomach cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

4. Colon cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

5. Uterine cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

6. Cervical cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

7. Breast cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

8. Thyroid cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

9. Kidney cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

10. Liver cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

11. Pancreas cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

12. Prostate cancer. Carcinogenesis. Precancerous conditions. Classification. Macroscopic forms. Histological types. Metastatic pathways. Complications and causes of death.

COURSE OF THE SESSION

Lung cancer

Carcinogenesis:

The development of lung carcinomas, commonly associated with malignancies such as adenocarcinoma, squamous cell carcinoma, and small cell carcinoma, follows a multistep process known as carcinogenesis. The initiation stage involves exposure to carcinogens, often tobacco smoke, which induces genetic mutations, particularly in tumor suppressor genes (e.g., TP53) and oncogenes (e.g., KRAS). Subsequent promotion stages involve clonal expansion of initiated cells, leading to the formation of preneoplastic lesions. Continued exposure to carcinogens can further drive progression to full malignancy, marked by uncontrolled cell proliferation and evasion of apoptosis.

Precancerous Conditions:

Lung carcinogenesis may manifest as precancerous lesions, such as squamous metaplasia, dysplasia, or carcinoma in situ, which precede invasive carcinoma. Chronic obstructive pulmonary disease (COPD), bronchial dysplasia, and pulmonary fibrosis are examples of precancerous conditions associated with an increased risk of lung carcinoma development.

Classification:

Lung carcinomas are classified into two main groups: non-small cell lung carcinoma (NSCLC) and small cell lung carcinoma (SCLC). NSCLC comprises several histological subtypes, including adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Adenocarcinoma is the most common subtype and often arises in the peripheral lung regions, while squamous cell carcinoma is frequently associated with central airways. SCLC, characterized by rapid growth and early metastasis, accounts for a smaller percentage of cases and is often linked to paraneoplastic syndromes.

Macroscopic and Histological Types:

Macroscopically, lung carcinomas can present as well-defined masses, nodules, or infiltrative lesions.

Histologically, adenocarcinomas are characterized by glandular differentiation and may present as lepidic, acinar, or solid subtypes. Squamous cell carcinomas exhibit keratinization and squamous differentiation, while large cell carcinomas lack distinctive features. Small cell carcinomas are marked by small, round cells with scant cytoplasm and high mitotic activity.

Metastatic Pathways:

Lung carcinomas commonly metastasize via lymphatic and hematogenous routes. Lymphatic spread involves regional lymph nodes, with mediastinal nodes being primary sites for metastasis. Hematogenous dissemination, particularly in small cell carcinoma, can lead to distant metastases in organs like the liver, bone, and brain.

Complications and Causes of Death:

Complications of lung carcinomas can include local invasion into adjacent structures, causing airway obstruction, hemoptysis, or superior vena cava syndrome.

Metastases to distant organs can result in complications such as pathological fractures, neurologic deficits, or organ failure. The primary cause of death in lung carcinoma patients is often attributed to advanced disease stages at diagnosis, limiting treatment options and leading to widespread metastases. The aggressive nature of small cell carcinoma, with its propensity for early dissemination, contributes to the high mortality rates associated with lung carcinomas.

Esophageal cancer

Carcinogenesis:

Esophageal cancer, a malignancy originating in the esophageal epithelium, typically follows a complex process of carcinogenesis. The primary risk factors include chronic irritation from long-term exposure to factors like tobacco and alcohol consumption, as well as gastroesophageal reflux disease (GERD). Carcinogenesis involves the accumulation of genetic mutations, notably in tumor suppressor genes like TP53 and oncogenes such as KRAS. Progression to invasive cancer is marked by the acquisition of additional genetic alterations that confer growth advantages to neoplastic cells.

Precancerous Conditions:

Esophageal cancer often arises from precursor lesions, including Barrett's esophagus, a metaplastic condition characterized by the replacement of normal squamous epithelium with columnar epithelium containing goblet cells. Barrett's esophagus is associated with chronic GERD and increases the risk of adenocarcinoma. Other precancerous conditions include squamous dysplasia, often linked to chronic irritation from factors like smoking and alcohol consumption.

Classification:

Esophageal cancer is broadly classified into two main types: esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC). ESCC is commonly associated with tobacco and alcohol use and typically occurs in the upper and middle thirds of the esophagus. EAC, on the other hand, is often linked to Barrett's esophagus and GERD, predominantly affecting the lower third of the esophagus.

Macroscopic and Histological Types:

Macroscopically, esophageal cancers may present as polypoid masses, ulcerative lesions, or infiltrative tumors.

Histologically, ESCC is characterized by squamous differentiation, often presenting as keratin pearls or intercellular bridges. EAC, derived from glandular epithelium, exhibits various patterns, including tubular, papillary, and mucinous structures.

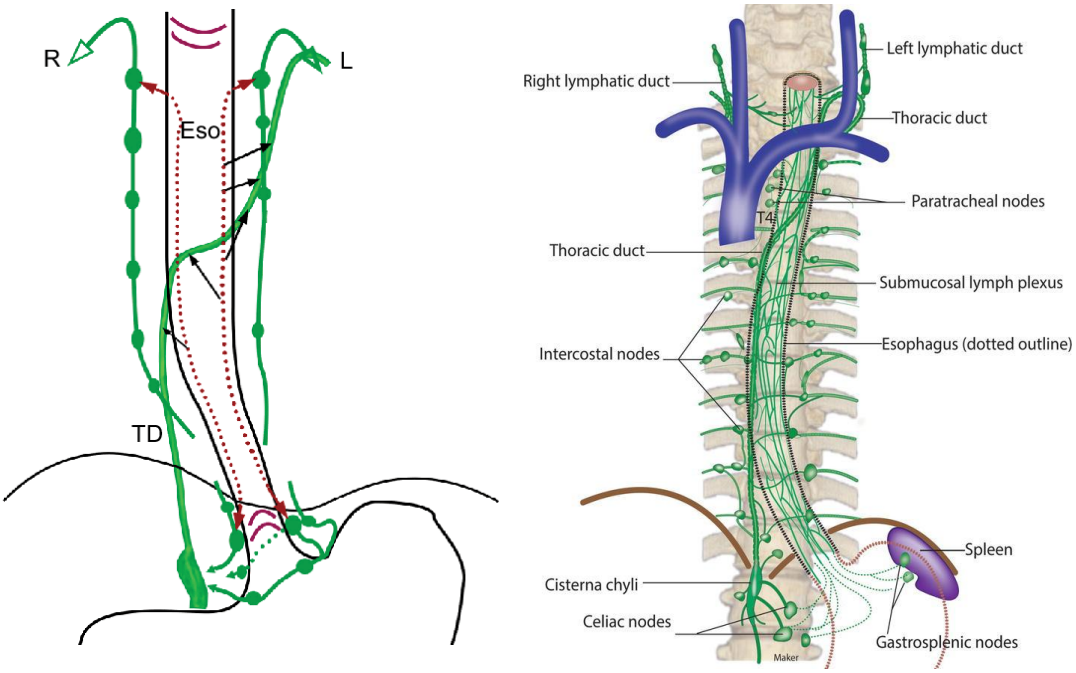
Metastatic Pathways:

Esophageal cancers have distinct metastatic pathways. Lymphatic spread is common, involving regional lymph nodes such as the mediastinal and celiac nodes. Hematogenous dissemination may occur, with distant metastases observed in organs like the liver, lungs, and bones.

Complications and Causes of Death:

Complications of esophageal cancer can include local invasion into adjacent structures, causing dysphagia, pain, or bleeding. The tumor may also obstruct the esophagus, leading to weight loss and malnutrition. Metastases can result in distant organ dysfunction. The primary cause of death in esophageal cancer patients is often related to advanced disease stages at diagnosis, limiting curative treatment options. Factors such as the presence of metastases, tumor location, and patient comorbidities influence the overall prognosis.

Lymphatic drainage of esophagus



Stomach cancer

Carcinogenesis:

Stomach cancer, or gastric cancer, undergoes a multistep process of carcinogenesis, often influenced by environmental and genetic factors. Chronic infection with Helicobacter pylori, a bacterium that colonizes the gastric mucosa, is a significant risk factor for gastric cancer development. Carcinogenesis involves the accumulation of genetic mutations, with alterations in tumor suppressor genes (e.g., TP53) and oncogenes (e.g., HER2) playing key roles.

Precancerous Conditions:

Several precancerous conditions precede the development of stomach cancer. Chronic atrophic gastritis, often associated with H. pylori infection, leads to the loss of glandular tissue in the stomach lining. Intestinal metaplasia, characterized by the replacement of normal gastric epithelium with intestinal-like epithelium, is another precursor. Dysplasia in the gastric mucosa represents a more advanced precancerous state, with the potential for progression to invasive adenocarcinoma.

Classification:

Stomach cancer is classified into different types, with adenocarcinoma being the predominant histological subtype. Lauren classification categorizes gastric adenocarcinoma into intestinal and diffuse types based on histological patterns. The World Health Organization (WHO) classification further refines the classification, considering factors such as mucin production and growth patterns. Other rare histological subtypes include signet ring cell carcinoma and mucinous adenocarcinoma.

Macroscopic and Histological Types:

Macroscopically, stomach cancers may present as polypoid masses, ulcerative lesions, or diffusely infiltrative tumors.

Histologically, intestinal-type adenocarcinoma is characterized by glandular structures with tubular or papillary architecture. In contrast, diffuse-type adenocarcinoma exhibits poorly cohesive cells with a discohesive growth pattern, often containing signet ring cells. These distinct histological patterns impact the tumor's behavior, response to therapy, and overall prognosis.

Metastatic Pathways:

Stomach cancer commonly metastasizes through both lymphatic and hematogenous pathways. Lymphatic spread involves regional lymph nodes, including the perigastric, celiac, and para-aortic nodes. Hematogenous dissemination may lead to distant metastases in organs such as the liver, lungs, and peritoneum.

Complications and Causes of Death:

Complications of stomach cancer include local invasion into adjacent structures, causing symptoms such as abdominal pain, dysphagia, and gastrointestinal bleeding. Tumor-related obstruction may result in gastric outlet obstruction and weight loss. Peritoneal dissemination can lead to carcinomatosis, causing ascites and abdominal pain. The primary cause of death in stomach cancer patients is often attributed to advanced disease stages at the time of diagnosis, limiting curative treatment options. Factors such as the extent of metastasis, tumor location, and patient comorbidities influence overall prognosis.

Colon cancer

Carcinogenesis:

Colon cancer, also known as colorectal cancer, arises through a stepwise process of carcinogenesis involving genetic and environmental factors. Most cases originate from adenomatous polyps, precancerous growths in the colon. Mutations in key genes, such as APC, KRAS, and TP53, play crucial roles in the transformation of normal colonic epithelial cells into cancerous cells.

Precancerous Conditions:

Adenomatous polyps like traditional serrated adenomas (TSA), tubular and villous adenomas serve as precancerous conditions in the development of colon cancer. These polyps may progress to carcinoma if left untreated.

Other precancerous conditions include inflammatory bowel diseases like ulcerative colitis and Crohn's disease, which predispose individuals to an increased risk of colorectal cancer.

Classification:

Colon cancer is broadly classified into two main types: adenocarcinoma and neuroendocrine tumors. Adenocarcinoma is the most common histological subtype, representing the majority of cases. This type originates from the glandular epithelial cells lining the colon. Within adenocarcinoma, molecular classification based on the presence of specific genetic alterations, such as microsatellite instability (MSI) or the CpG island methylator phenotype (CIMP), provides additional insights into prognosis and potential treatment strategies.

Macroscopic and Histological Types:

Macroscopically, colon cancers can present as polypoid masses, ulcerative lesions, or infiltrative tumors.

Histologically, adenocarcinoma is characterized by glandular differentiation, typically forming tubular or cribriform structures. Mucinous adenocarcinoma is a subtype characterized by abundant extracellular mucin production. Signet ring cell carcinoma is another variant with cells containing intracytoplasmic mucin. The specific histological features impact the tumor's behavior, response to treatment, and overall prognosis.

Metastatic Pathways:

Colon cancer commonly metastasizes through the lymphatic and hematogenous pathways. Lymphatic spread involves regional lymph nodes, particularly those along the mesenteric vessels. Hematogenous dissemination may lead to distant metastases, commonly affecting the liver, lungs, and peritoneum.

Complications and Causes of Death:

Complications of colon cancer can include local invasion into adjacent structures, causing symptoms such as abdominal pain, changes in bowel habits, and gastrointestinal bleeding. Obstruction of the colon may result in bowel obstruction and abdominal distension. Perforation of the colon can lead to peritonitis, a severe and potentially life-threatening complication. The primary cause of death in colon cancer patients is often attributed to advanced disease stages at the time of diagnosis, limiting curative treatment options. Factors such as the extent of metastasis, tumor location, and patient comorbidities influence overall prognosis.

Uterine cancer

Carcinogenesis:

Uterine cancer, primarily arising from the endometrium, undergoes a complex process of carcinogenesis. The most common type of uterine cancer is endometrial carcinoma. Carcinogenesis in endometrial cancer is often associated with hormonal influences, particularly unopposed estrogen exposure without progesterone. Genetic mutations in key pathways, such as PTEN and KRAS, contribute to the dysregulation of cell proliferation and apoptosis. Endometrial hyperplasia, a precancerous condition characterized by excessive growth of endometrial cells, represents an intermediate step in the progression to endometrial carcinoma.

Precancerous Conditions:

Endometrial hyperplasia is a significant precancerous condition in the context of uterine cancer. It encompasses a spectrum ranging from simple hyperplasia to

complex atypical hyperplasia, the latter being associated with a higher risk of progression to malignancy. Other risk factors for uterine cancer include obesity, diabetes, and certain hormonal conditions.

Classification:

Uterine cancers are broadly classified into two main types: endometrial carcinoma and uterine sarcoma. Endometrial carcinoma is the more prevalent histological subtype, and it is further classified into two main types based on histological features: Type I, which is estrogen-related and includes endometrioid adenocarcinoma, and Type II, which is estrogen-independent and includes serous carcinoma and clear cell carcinoma. Uterine sarcomas, although less common, represent a heterogeneous group of mesenchymal tumors that can arise from the myometrium or endometrial stroma.

Macroscopic and Histological Types:

Macroscopically, uterine cancers may present as polypoid masses, infiltrative lesions, or diffusely thickened endometrium.

Histologically, endometrioid adenocarcinoma is characterized by glandular structures resembling the normal endometrium. Serous carcinoma, a more aggressive subtype, displays papillary structures and often lacks the glandular architecture seen in endometrioid adenocarcinoma. Clear cell carcinoma is characterized by clear cytoplasm and may have a distinct histological appearance.

Uterine sarcomas, which include leiomyosarcoma and endometrial stromal sarcoma, have different histological features reflecting their mesenchymal origin.

Metastatic Pathways:

Uterine cancers commonly metastasize through lymphatic and hematogenous pathways. Lymphatic spread involves regional lymph nodes, particularly those in the pelvis. Hematogenous dissemination may lead to distant metastases, commonly affecting the lungs, liver, and bones.

Complications and Causes of Death:

Complications of uterine cancer can include local invasion into adjacent structures, causing symptoms such as abnormal uterine bleeding, pelvic pain, and urinary symptoms. Uterine cancers can also lead to complications such as bowel obstruction or ureteral obstruction. The primary cause of death in uterine cancer patients is often attributed to advanced disease stages at diagnosis, limiting curative treatment options. Factors such as the extent of metastasis, tumor type, and patient comorbidities influence overall prognosis.

Cervical cancer

Carcinogenesis:

Cervical cancer, predominantly associated with persistent infection by high-risk human papillomavirus (HPV) types, undergoes a stepwise process of carcinogenesis. HPV infection is a major risk factor, leading to the integration of viral DNA into the host genome and subsequent dysregulation of cell cycle control. Key oncogenes, such as E6 and E7, encoded by high-risk HPV, play a pivotal role in the transformation of normal cervical epithelial cells into malignant cells.

Precancerous Conditions:

Precancerous conditions of the cervix primarily manifest as cervical intraepithelial neoplasia (CIN), graded from CIN 1 (low-grade squamous intraepithelial neoplasia or SIL) to CIN 2-3 (high-grade SIL) and carcinoma in situ. Persistent infection with high-risk HPV types is a common precursor to CIN. CIN lesions represent various degrees of dysplasia in the cervical epithelium, and the risk of progression to invasive cervical cancer is directly associated with the severity of dysplasia. Regular screening, particularly through Pap smears and HPV testing, is crucial for the early detection and management of precancerous conditions.

Classification:

Cervical cancers are classified based on histological features into squamous cell carcinoma and adenocarcinoma, with squamous cell carcinoma being the more prevalent type. Squamous cell carcinoma typically arises from the squamous epithelial cells lining the cervix and is often associated with HPV infection. Adenocarcinoma arises from glandular cells in the cervical canal and is frequently linked to persistent HPV infection as well.

Macroscopic and Histological Types:

Macroscopically, cervical cancers may present as exophytic or endophytic lesions, infiltrative masses, or ulcerative tumors.

Histologically, squamous cell carcinoma is characterized by nests of malignant squamous epithelial cells displaying various degrees of differentiation. Well-differentiated tumors exhibit keratinization, while poorly differentiated tumors may lack this feature. Adenocarcinoma is characterized by malignant glandular structures, often forming complex or papillary patterns.

Metastatic Pathways:

Cervical cancer commonly metastasizes through lymphatic and hematogenous pathways. Lymphatic spread involves regional lymph nodes, particularly those in the pelvis. Hematogenous dissemination may lead to distant metastases, commonly affecting the lungs, liver, and bones.

Complications and Causes of Death:

Complications of cervical cancer can include local invasion into adjacent structures, causing symptoms such as abnormal vaginal bleeding, pelvic pain, and urinary symptoms. Advanced cervical cancer may lead to complications such as ureteral obstruction, bowel obstruction, or hydronephrosis. The primary cause of death in cervical cancer patients is often attributed to advanced disease stages at diagnosis, limiting curative treatment options. Factors such as the extent of metastasis, histological type, and patient comorbidities influence overall prognosis.

Breast cancer

Carcinogenesis:

Breast cancer, a heterogeneous malignancy arising from the epithelial cells of the mammary glands, undergoes a complex process of carcinogenesis. The majority of breast cancers are ductal carcinomas, and the development of these tumors is influenced by both genetic and environmental factors. Genetic mutations in tumor suppressor genes like BRCA1 and BRCA2, as well as oncogenes such as HER2, can contribute to the initiation and progression of breast cancer. Hormonal influences,

particularly estrogen and progesterone, play a critical role in the carcinogenesis of hormone receptor-positive breast cancers.

Precancerous Conditions:

Precancerous conditions in the breast include ductal carcinoma in situ (DCIS), characterized by the presence of abnormal cells within the ducts that have not invaded surrounding tissues. Lobular carcinoma in situ (LCIS) is another precursor, involving abnormal growth within the lobules. Atypical hyperplasia represents a more generalized abnormal proliferation of breast cells.

Classification:

Breast cancers are broadly classified into several types based on the expression of hormone receptors (estrogen and progesterone receptors), HER2 status, and histological features. The main subtypes include hormone receptor-positive (ER/PR+), HER2-positive, triple-negative (ER/PR-/HER2-), and luminal subtypes. Molecular classification, such as the PAM50 gene expression assay, further refines categorization based on intrinsic biological subtypes, including Luminal A, Luminal B, HER2-enriched, and Basal-like.

Macroscopic and Histological Types:

Macroscopically, breast cancers may present as well-defined masses, irregular nodules, or diffusely infiltrative lesions.

Histologically, invasive ductal carcinoma (IDC) is the most common type, characterized by malignant cells infiltrating the breast stroma. Invasive lobular carcinoma (ILC) arises from the lobules and has a characteristic growth pattern involving single-file infiltration. Other histological types include mucinous carcinoma, medullary carcinoma, and tubular carcinoma, each with distinct histological features influencing tumor behavior and prognosis.

Metastatic Pathways:

Breast cancer commonly metastasizes through lymphatic and hematogenous pathways. Lymphatic spread involves regional lymph nodes, particularly the axillary nodes. Hematogenous dissemination may lead to distant metastases, commonly affecting bones, lungs, liver, and brain.

Complications and Causes of Death:

Complications of breast cancer can include local invasion into adjacent structures, causing symptoms such as breast pain, changes in breast appearance, and skin changes. Advanced breast cancer may lead to complications such as bone metastases causing fractures, lung metastases causing respiratory distress, or brain metastases causing neurological symptoms. The primary cause of death in breast cancer patients is often attributed to advanced disease stages at diagnosis, limiting curative treatment options. Factors such as the extent of metastasis, tumor subtype, and patient comorbidities influence overall prognosis.

Thyroid cancer

Carcinogenesis:

Thyroid cancer, originating from the thyroid follicular cells, undergoes a complex process of carcinogenesis. The majority of thyroid cancers are of epithelial origin, with well-differentiated subtypes being the most common. The main driver

mutations in thyroid cancer include alterations in the MAP kinase pathway, such as mutations in the BRAF and RAS genes. Exposure to ionizing radiation, particularly during childhood, is a well-established risk factor for thyroid cancer.

Precancerous Conditions:

Thyroid nodules with dysplasia, particularly those showing features of follicular epithelial cell proliferation, can be considered precancerous conditions. Additionally, chronic thyroiditis, such as Hashimoto's thyroiditis, has been associated with an increased risk of thyroid cancer, particularly papillary thyroid carcinoma. The presence of precursor lesions highlights the importance of careful evaluation and monitoring of thyroid nodules, especially those with suspicious features on imaging or fine-needle aspiration.

Classification:

Thyroid cancers are broadly classified into differentiated thyroid cancers (DTC), medullary thyroid carcinoma (MTC), and anaplastic thyroid carcinoma (ATC). DTC, which includes papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC), constitutes the majority of thyroid cancers and is associated with a favorable prognosis. MTC arises from the parafollicular C cells and may be sporadic or hereditary, often related to mutations in the RET proto-oncogene. ATC is an aggressive and undifferentiated subtype with a poor prognosis.

Macroscopic and Histological Types:

Macroscopically, thyroid cancers may present as well-defined nodules, irregular masses, or diffusely infiltrative lesions.

Histologically, PTC is characterized by papillary structures, nuclear features such as nuclear grooves and pseudoinclusions, and a slow-growing behavior. FTC often forms follicular structures and may invade blood vessels, while Hürthle cell carcinoma is a variant of FTC composed of oncocytic cells. MTC is identified by nests and sheets of C cells with amyloid deposits. ATC is characterized by undifferentiated and highly pleomorphic cells lacking the characteristic features of well-differentiated thyroid cancers.

Metastatic Pathways:

Thyroid cancer commonly metastasizes through lymphatic and hematogenous pathways. Lymphatic spread involves regional lymph nodes, particularly those in the central compartment of the neck. Hematogenous dissemination may lead to distant metastases, commonly affecting the lungs and bones.

Complications and Causes of Death:

Complications of thyroid cancer can include local invasion into adjacent structures, causing symptoms such as difficulty swallowing, voice changes, and neck pain. Advanced thyroid cancer may lead to complications such as tracheal or esophageal compression, distant organ metastases causing organ dysfunction, or recurrent laryngeal nerve involvement causing vocal cord paralysis. The primary cause of death in thyroid cancer patients is often associated with advanced disease stages at diagnosis, particularly in cases of anaplastic thyroid carcinoma. Factors such as the extent of metastasis, tumor subtype, and patient comorbidities influence overall prognosis.

Kidney cancer

Carcinogenesis:

Kidney cancer, predominantly renal cell carcinoma (RCC), originates from the renal tubular epithelium and undergoes a multifaceted process of carcinogenesis. The most common subtype, clear cell RCC, is often associated with genetic alterations in the von Hippel-Lindau (VHL) gene, leading to dysregulation of hypoxia-inducible factor (HIF) and subsequent angiogenesis. Other subtypes, such as papillary and chromophobe RCC, have distinct genetic and molecular profiles. Environmental factors, including smoking and exposure to certain chemicals, may contribute to the development of kidney cancer.

Precancerous Conditions:

The concept of precancerous lesions in kidney cancer is less defined compared to some other cancers. Renal cysts, particularly complex renal cysts with irregularities, may be considered precancerous conditions as they can occasionally harbor renal cell carcinoma. Additionally, individuals with certain genetic syndromes, such as von Hippel-Lindau (VHL) disease, have an increased risk of developing kidney cancer.

Classification:

Kidney cancers are classified into several histological subtypes, with clear cell RCC, papillary RCC, and chromophobe RCC being the most common. Clear cell RCC is characterized by clear cytoplasm due to lipid and glycogen accumulation. Papillary RCC is identified by papillary structures, and chromophobe RCC exhibits large pale cells with a distinctive perinuclear halo. Other rare subtypes, including collecting duct carcinoma and renal medullary carcinoma, are characterized by unique histological features.

Macroscopic and Histological Types:

Macroscopically, kidney cancers may present as well-defined masses, irregular nodules, or infiltrative lesions within the renal parenchyma.

Histologically, clear cell RCC is characterized by nests or sheets of clear cells with a rich vascular network. Papillary RCC exhibits papillary structures with fibrovascular cores, while chromophobe RCC displays large cells with prominent cell membranes. Collecting duct carcinoma is characterized by infiltrating tubules and cribriform patterns, and renal medullary carcinoma often presents as aggressive and poorly differentiated tumors.

Metastatic Pathways:

Kidney cancer commonly metastasizes through both lymphatic and hematogenous pathways. Lymphatic spread involves regional lymph nodes, particularly those around the renal hilum. Hematogenous dissemination may lead to distant metastases, commonly affecting the lungs, bones, and liver.

Complications and Causes of Death:

Complications of kidney cancer can include local invasion into adjacent structures, causing symptoms such as flank pain, hematuria, and abdominal mass. Advanced kidney cancer may lead to complications such as venous thrombosis, tumor rupture, or distant organ metastases causing organ dysfunction. The primary cause of death in kidney cancer patients is often associated with advanced disease

stages at diagnosis, limiting curative treatment options. Factors such as the extent of metastasis, tumor subtype, and patient comorbidities influence overall prognosis. Multidisciplinary approaches, including surgery, targeted therapies (e.g., tyrosine kinase inhibitors), and immune checkpoint inhibitors, aim to optimize outcomes, emphasizing the importance of early detection and tailored therapeutic interventions in kidney cancer management.

Liver cancer

Carcinogenesis:

Liver cancer, predominantly hepatocellular carcinoma (HCC), arises from hepatocytes and undergoes a multistep process of carcinogenesis. Chronic liver inflammation, often due to viral hepatitis (hepatitis B or C), alcoholic liver disease, or non-alcoholic fatty liver disease (NAFLD), plays a significant role in the development of HCC. The continuous cycle of liver cell injury, inflammation, and regeneration contributes to genetic and epigenetic alterations that promote hepatocarcinogenesis. Key genetic changes include mutations in the TP53 tumor suppressor gene and activation of oncogenes such as CTNNB1 (beta-catenin). Cirrhosis, a consequence of chronic liver disease, is a well-established precancerous condition, providing a milieu conducive to the development of HCC.

Precancerous Conditions:

Cirrhosis is the most notable precancerous condition for liver cancer. It is a consequence of long-term liver damage and inflammation, leading to fibrosis and distortion of liver architecture. Cirrhosis is often associated with chronic viral hepatitis, alcoholic liver disease, NAFLD, and other liver disorders. In the cirrhotic liver, nodules of regenerating hepatocytes may undergo dysplastic changes, eventually progressing to HCC.

Classification:

Liver cancers are broadly classified into primary liver cancers, primarily HCC, and secondary liver cancers, which are metastases from other primary sites. HCC accounts for the majority of primary liver cancers and can be further classified based on the underlying liver disease, such as cirrhosis-associated HCC or non-cirrhotic HCC. Rare subtypes of primary liver cancer include fibrolamellar carcinoma and hepatic angiosarcoma. Secondary liver cancers, commonly metastatic from the gastrointestinal tract (e.g., colorectal cancer) or other organs, have distinct histological features that differ from primary liver cancers.

Macroscopic and Histological Types:

Macroscopically, HCC may present as a solitary mass, multiple nodules, or diffuse infiltrative lesions within the liver parenchyma. Histologically, HCC is characterized by trabecular or pseudoglandular structures formed by malignant hepatocytes. The tumor cells may exhibit nuclear atypia, increased mitotic activity, and architectural disarray. Fibrolamellar carcinoma is a rare variant characterized by dense fibrous bands. Hepatic angiosarcoma, another rare subtype, arises from the hepatic blood vessels and has a distinct histological appearance with atypical endothelial cells.

Metastatic Pathways:

Liver cancer commonly metastasizes through hematogenous pathways, as the liver receives blood from both the hepatic artery and the portal vein. The portal vein is a common route for metastases from the gastrointestinal tract, while the hepatic artery supplies the liver with oxygenated blood and may carry metastatic cells from other primary sites.

Complications and Causes of Death:

Complications of liver cancer can include local invasion into adjacent structures, causing symptoms such as abdominal pain, jaundice, and ascites. Advanced liver cancer may lead to complications such as portal vein thrombosis, hepatic encephalopathy, or distant organ metastases causing organ dysfunction. The primary cause of death in liver cancer patients is often associated with advanced disease stages at diagnosis, limiting curative treatment options. Factors such as the extent of metastasis, tumor subtype, and underlying liver function influence overall prognosis.

Pancreas cancer

Carcinogenesis

Pancreatic cancer primarily arises through a multistep process of genetic and epigenetic alterations leading to malignant transformation of the pancreatic epithelium. Key driver mutations in pancreatic ductal adenocarcinoma (PDAC), the most common form, include KRAS activation and inactivation of tumor suppressor genes such as TP53, CDKN2A (p16), and SMAD4. The carcinogenic process often begins with pancreatic intraepithelial neoplasia (PanIN), which progresses through low-grade to high-grade dysplasia before evolving into invasive carcinoma. Chronic inflammation, oxidative stress, and stromal remodeling also contribute to the carcinogenic microenvironment.

Precancerous conditions

Several lesions are recognized as precursors to pancreatic cancer. These include PanINs, intraductal papillary mucinous neoplasms (IPMNs), mucinous cystic neoplasms (MCNs), and less commonly, solid pseudopapillary neoplasms. Chronic pancreatitis—particularly hereditary or due to long-standing alcohol use—and cystic fibrosis are considered risk conditions for malignancy due to prolonged epithelial damage and regeneration. Patients with familial pancreatic cancer syndromes or hereditary mutations (e.g., BRCA2, STK11) also face higher risk.

Classification

Pancreatic cancers are classified based on their cell of origin. The majority (over 90%) are ductal adenocarcinomas. Less frequent forms include acinar cell carcinoma, pancreatoblastoma (mainly in children), and neuroendocrine tumors (NETs), which vary from well-differentiated NETs to poorly differentiated neuroendocrine carcinomas. The WHO classification also considers tumor grade and differentiation, which bear prognostic significance. Pancreatic cancers may also be staged anatomically using the TNM system, which assesses tumor size, lymph node involvement, and metastasis.

Macroscopic and Histological Types

Macroscopic types of pancreatic ductal adenocarcinoma typically present as ill-defined, hard, gray-white masses in the pancreatic head, often encasing surrounding vessels and bile ducts. Histologically, these tumors are composed of irregular, infiltrating duct-like structures within a dense desmoplastic stroma. High mitotic activity, cellular atypia, and perineural invasion are common. Mucinous and anaplastic variants exist, with the latter exhibiting more aggressive behavior. Neuroendocrine tumors, by contrast, show nested or trabecular growth patterns with characteristic chromogranin and synaptophysin positivity on immunohistochemistry.

Metastatic Pathways

Pancreatic cancer spreads early and aggressively. Lymphatic spread occurs to peripancreatic, celiac, and mesenteric nodes. Hematogenous dissemination frequently targets the liver via the portal vein and the lungs via systemic circulation. Peritoneal seeding and direct invasion of adjacent structures (e.g., duodenum, stomach, spleen) are also common. In advanced cases, bone and brain metastases can occur, though less frequently. Neural invasion, a hallmark of pancreatic cancer, contributes to early pain symptoms and local recurrence.

Complications and Causes of Death

Complications arise from both local tumor growth and systemic effects. Biliary obstruction due to tumor compression in the pancreatic head leads to jaundice and cholangitis. Duodenal obstruction and pancreatic exocrine insufficiency contribute to malnutrition and cachexia. Tumor invasion of vascular structures can cause bleeding or thrombosis. Systemic effects include paraneoplastic syndromes and progressive metastasis. Most deaths result from widespread metastatic disease, liver failure, cachexia, or sepsis. The prognosis remains extremely poor, with a five-year survival rate below 10%, emphasizing the need for early detection and novel therapeutic approaches.

Prostate cancer

Carcinogenesis

Prostate cancer develops through a series of molecular events involving genetic, hormonal, and environmental factors. The carcinogenesis process is often initiated by mutations in oncogenes such as MYC and inactivation of tumor suppressor genes including PTEN, TP53, and RB1. Androgen receptor (AR) signaling plays a central role, driving cell proliferation and survival; thus, prostate cancer is highly hormone-dependent, particularly in its early stages. Epigenetic changes, such as DNA methylation and histone modification, also contribute to neoplastic transformation. The fusion of TMPRSS2 with ETS family transcription factors (especially ERG) is a common early event.

Precancerous Conditions

The principal recognized precancerous lesion for prostate cancer is high-grade prostatic intraepithelial neoplasia (HGPIN), characterized by architectural and cytological atypia within prostatic ducts and acini without stromal invasion. While HGPIN is not an obligate precursor, it is often found adjacent to carcinomas and is considered a marker of increased cancer risk. Atypical small acinar proliferation

(ASAP) is another suspicious finding that may reflect early invasive cancer. Chronic inflammation and proliferative inflammatory atrophy (PIA) are also proposed as potential early lesions that may evolve into HGPIN and eventually carcinoma.

Classification

Prostate cancers are broadly classified based on their cellular origin and differentiation. The overwhelming majority are adenocarcinomas of the acinar type, arising from the glandular epithelium. Rarer forms include ductal adenocarcinoma, small cell carcinoma (a type of neuroendocrine tumor), squamous cell carcinoma, and sarcomas. Tumors are graded histologically using the Gleason grading system, now incorporated into the ISUP Grade Group system, ranging from Grade Group 1 (least aggressive) to Grade Group 5 (most aggressive). Staging follows the TNM system, considering tumor extent, lymph node involvement, and distant metastasis.

Macroscopic and Histological Types

Macroscopically, prostate cancer often appears as a firm, poorly defined area within the peripheral zone of the posterior prostate, typically affecting the posterior and lateral lobes. The tumor may be multifocal and not readily visible grossly. Histologically, conventional acinar adenocarcinoma shows small, crowded glands with a single layer of atypical epithelial cells, lacking basal cells—a key diagnostic feature. Higher-grade tumors display fused glands, cribriform patterns, or sheets of undifferentiated cells. Perineural invasion is common. Ductal adenocarcinomas show papillary or cribriform architecture and present more aggressively.

Metastatic Pathways

Prostate cancer primarily spreads via local extension, lymphatics, and hematogenous routes. Locally, it invades seminal vesicles, bladder neck, and pelvic soft tissues. Lymphatic spread occurs to pelvic lymph nodes, particularly obturator and iliac groups. Hematogenous dissemination frequently targets the axial skeleton—spine, pelvis, and femur—resulting in characteristic osteoblastic (bone-forming) metastases. Visceral metastases to liver and lungs may occur in advanced stages, especially in high-grade or variant histologies like small cell carcinoma.

Complications and Causes of Death

Complications of prostate cancer arise from local progression and distant metastases. Locally advanced tumors may cause urinary retention, hematuria, or obstructive uropathy leading to hydronephrosis and renal failure. Bone metastases result in pain, pathological fractures, spinal cord compression, and hypercalcemia in some cases. Androgen deprivation therapy (ADT), the cornerstone of treatment, can lead to metabolic complications. Death usually results from complications of metastases—particularly skeletal involvement—or from treatment-resistant castration-resistant prostate cancer (CRPC). Visceral organ failure or cachexia also contributes to mortality in terminal stages.

INFORMATIONAL AND METHODOLOGICAL PART

MAIN LITERATURE

1. Pathomorphology : textbook / ed. by I.V. Sorokina, V.D. Markovskyi, D.I. Halata. - 2nd ed. - Kyiv : AUS Medicine Publishing, 2020. - 327 p., [10] col. inserts : tab.

2. Klatt, E. C. Robbins and Cotran Atlas of Pathology : [with Student Consult Online Access] / Edward C. Klatt. - third edition. - Philadelphia : Elsevier, 2015. - 587 p. : il.

3. Robbins Basic pathology / [ed. by] Vinay Kumar, Abul K. Abbas, Jon C. Aster. - 9th ed. - [Philadelphia] : Elsevier ; Saunders. - 910 p. : ill., scheme, tab.

ADDITIONAL LITERATURE

1. Sobotta. Atlas of human anatomy. [V. 1]. General anatomy and musculoskeletal system / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 400 p. : ill., col. ill.

2. Sobotta. Atlas of human anatomy. [V. 2]. Internal organs / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 259 p. : ill., col. ill.

3. Sobotta. Atlas of human anatomy. [V. 3]. Head, neck, and neuroanatomy / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 370 p. : ill., col. ill.

4. Weir & Abrahams' imaging atlas of human anatomy / ed.: J. D. Spratt [and oth.] ; consultant eds.: J. Weir, P. H. Abrahams. – 5th ed. - [S.l.] : Elsevier, 2017. - xvi, 263 p. : ill.

NORMATIVE LEGAL ACTS AND DOCUMENTS

1. Order of the Ministry of Health of the Republic of Belarus No. 111 of 06/01/1993 "On further improvement of the pathological service of the Republic of Belarus"

Access mode: http://patan.by/menyu/administrativnyie-proczeduryi.html - The date fccess: 20.03.2022.

ELECTRONIC DATABASES

1. Physician's consultant. Electronic Medical Library = Consultant of the doctor. Electronic medical library [Electronic resource] / Publishing group "GEOTAR-Media", LLC "IPUZ". – Access mode: http://www.rosmedlib.ru/ . – Access date: 03/15/2022.

2. Springer Link [Electronic resource] / Springer International Publishing AG. – Access mode: https:link.springer.com. – Date of access: 03/15/2022.