

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

Department of Pathological Anatomy

Author:

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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: “Iatrogenesis”

Duration: 3 hours

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

Educational Goal:

- To study the definition, classification, etiology, pathogenesis, morphology, clinical presentation, complications, and outcomes of iatrogenic conditions. To define iatrogenesis as any adverse condition or complication resulting from medical intervention (diagnostic, therapeutic, or preventive) rather than the underlying disease itself. To analyze the classification of iatrogenic conditions: diagnostic iatrogenesis (complications of biopsy, endoscopy, angiography, lumbar puncture – bleeding, infection, perforation, pneumothorax, nerve injury), therapeutic iatrogenesis (drug-induced, surgical, radiation-induced), medication-related (adverse drug reactions – ADRs; medication errors; polypharmacy; drug-drug interactions; specific drug toxicities: chemotherapy (myelosuppression, cardiotoxicity – anthracyclines, pulmonary fibrosis – bleomycin, hemorrhagic cystitis – cyclophosphamide, peripheral neuropathy – vincristine, cisplatin), antibiotics (nephrotoxicity – aminoglycosides, vancomycin; ototoxicity; pseudomembranous colitis – clindamycin, cephalosporins, fluoroquinolones; Stevens-Johnson syndrome – sulfonamides, anticonvulsants, allopurinol), NSAIDs (gastropathy, nephropathy), anticoagulants (bleeding), corticosteroids (immunosuppression, osteoporosis, avascular necrosis, Cushing syndrome, adrenal suppression), opioids (respiratory depression, constipation), contrast media (nephropathy, anaphylaxis). To analyze surgical iatrogenesis: retained foreign bodies (gossypiboma – retained surgical sponge; surgical instrument), wrong-site surgery, anesthetic complications (malignant hyperthermia, awareness, aspiration), postoperative infections (surgical site infection – SSI; nosocomial pneumonia; catheter-related bloodstream infection – CRBSI; urinary tract infection – CAUTI), thromboembolic complications (deep vein thrombosis, pulmonary embolism), anastomotic leak, postoperative hemorrhage, nerve injury, transfusion-related complications (transfusion reactions: acute hemolytic, febrile, allergic, transfusion-related acute lung injury – TRALI, transfusion-associated circulatory overload – TACO, infectious transmission). To analyze radiation-induced iatrogenesis (see Topic 35). To examine hospital-acquired (nosocomial) infections: Clostridioides difficile colitis, ventilator-associated pneumonia (VAP), central line-associated bloodstream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), surgical site infection (SSI), multidrug-resistant organisms (MRSA, VRE, ESBL, CRE). To discuss diagnostic errors: missed diagnosis, delayed diagnosis, incorrect diagnosis, overdiagnosis, false-positive/false-negative test results. To analyze medication errors: wrong drug, wrong dose, wrong route, wrong patient, wrong time, omission. To examine transfusion medicine complications (as above). To discuss contrast-induced nephropathy (CIN) and anaphylaxis. To analyze pressure ulcers (bedsores) as a complication of immobilization in

hospitalized patients. To discuss falls and injuries in healthcare settings. To examine psychological iatrogenesis: nocebo effect, anxiety induced by diagnosis or test results, stigmatization. To discuss prevention strategies: checklists (WHO Surgical Safety Checklist), medication reconciliation, clinical decision support systems, infection control protocols, hand hygiene, root cause analysis, adverse event reporting systems, quality improvement initiatives. To emphasize the role of the pathologist in recognizing and documenting iatrogenic conditions at autopsy and in biopsy specimens.

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 definition and classification of iatrogenic conditions;
- The adverse effects of common medications (chemotherapy, antibiotics, NSAIDs, anticoagulants, corticosteroids, opioids, contrast media);
- The morphological findings in drug-induced lung disease, liver injury, and nephrotoxicity;
- The complications of surgical interventions (retained foreign bodies, anastomotic leak, thromboembolism, nerve injury);
- The types of transfusion reactions (acute hemolytic, febrile, allergic, TRALI, TACO);
- The definition and examples of nosocomial infections;
- The concept of medication errors and diagnostic errors;
- Prevention strategies for iatrogenic events.

Be able to:

- Identify retained surgical sponges (gossypiboma) on macroscopic and microscopic examination;
- Recognize drug-induced tissue injury (chemotherapy effects on bone marrow, methotrexate hepatotoxicity, amiodarone pulmonary toxicity);
- Diagnose pathological processes and diseases based on the description of macroscopic and microscopic changes in organs and tissues of the body, including iatrogenic conditions;
- Distinguish resuscitation-related injuries from inflicted trauma at autopsy.

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;
- The ability to identify and document iatrogenic conditions in pathological specimens and at autopsy.

Motivation for Mastering the Topic:

Iatrogenesis – harm caused by medical intervention – is a major patient safety concern and a leading cause of morbidity and mortality in healthcare systems worldwide. It is estimated that preventable medical errors are among the top causes of death in developed countries. Adverse drug reactions, surgical complications, hospital-acquired infections, transfusion reactions, and diagnostic errors affect millions of patients annually. Understanding iatrogenic conditions is essential for all healthcare providers to recognize, prevent, and manage these complications. The pathologist plays a critical role in identifying iatrogenic injuries at autopsy (e.g., retained surgical sponges, unsuspected pneumothorax, drug toxicity) and in biopsy specimens (e.g., drug-induced liver injury, radiation changes). Knowledge of iatrogenesis is fundamental to medical ethics, quality improvement, risk management, and the delivery of safe, high-quality patient care. This topic also emphasizes the importance of transparency, disclosure, and learning from adverse events to improve healthcare systems.

QUESTIONS

1. Iatrogenic pathology. Definition. Examples. Morphology. Complications and outcomes. Causes of death.

COURSE OF THE SESSION

Iatrogenic pathology refers to any disease state, injury, or adverse condition directly caused by medical intervention, whether diagnostic, therapeutic, surgical, pharmacologic, or resulting from medical error. The term derives from the Greek words *iatros*, meaning physician, and *genesis*, meaning origin, and it encompasses both preventable errors and unavoidable complications of necessary medical care. Iatrogenic conditions may affect any organ system and can range from mild reversible effects to life-threatening or fatal outcomes. The study of iatrogenic pathology requires a thorough understanding of definition, classification, etiology, pathogenesis, morphology, clinical presentation, complications, and outcomes, as these conditions frequently prolong hospital stays, increase morbidity, reduce quality of life, and may lead to death.

Classification of iatrogenic conditions

Iatrogenic conditions are broadly classified according to the type of medical intervention that precipitates them. Diagnostic iatrogenesis refers to adverse events resulting from diagnostic procedures such as biopsy, endoscopy, angiography, and lumbar puncture. Complications of these procedures include bleeding at the puncture site, infection introduced by the instrument, perforation of a hollow viscus, pneumothorax following thoracic needle biopsy or central line placement, and nerve injury from improper needle placement. Therapeutic iatrogenesis encompasses complications arising from active treatment and is subdivided into drug-induced, surgical, and radiation-induced categories. Medication-related iatrogenesis includes adverse drug reactions, medication errors, polypharmacy, drug-drug interactions, and specific drug toxicities. Surgical iatrogenesis includes retained foreign bodies, wrong-site surgery, anesthetic complications, postoperative infections, thromboembolic events, anastomotic leaks, hemorrhage, nerve injury, and transfusion-related complications. Radiation-induced iatrogenesis produces both acute and chronic tissue damage. Hospital-acquired or nosocomial infections represent a major category of iatrogenic pathology, including *Clostridioides difficile* colitis, ventilator-associated pneumonia, central line-associated bloodstream infection, catheter-associated urinary tract infection, surgical site infection, and infections caused by multidrug-resistant organisms such as methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, extended-spectrum beta-lactamase-producing bacteria, and carbapenem-resistant *Enterobacteriaceae*.

Medication-related iatrogenesis: adverse drug reactions and toxicities

Adverse drug reactions represent a large proportion of iatrogenic pathology and can be either predictable or idiosyncratic. Chemotherapeutic agents produce a characteristic spectrum of toxicities due to their effects on rapidly dividing cells. Myelosuppression manifests as hypocellular bone marrow with pancytopenia, increasing the risk of infection and bleeding. Cardiotoxicity is a well-known complication of anthracyclines such as doxorubicin, where histopathological examination reveals vacuolar degeneration of cardiomyocytes, myofibrillar loss, and

ultimately irreversible dilated cardiomyopathy. Pulmonary fibrosis induced by bleomycin shows histologically as interstitial fibrosis with atypical type II pneumocytes and honeycombing in advanced cases. Hemorrhagic cystitis from cyclophosphamide results from acrolein metabolite injury to the urothelium, producing mucosal ulceration, hemorrhage, and chronic inflammation. Peripheral neuropathy from vincristine or cisplatin reflects axonal degeneration and demyelination, with clinical manifestations of sensory loss and motor weakness.

Antibiotics are associated with multiple iatrogenic injuries. Nephrotoxicity from aminoglycosides such as gentamicin and from vancomycin occurs through proximal tubular necrosis, histologically showing tubular epithelial cell swelling, vacuolization, and necrosis with sparing of the glomeruli. Ototoxicity from these same agents damages the hair cells of the cochlea and vestibular apparatus, leading to irreversible hearing loss and balance disorders. Pseudomembranous colitis caused by *Clostridioides difficile* is typically associated with clindamycin, cephalosporins, and fluoroquinolones; the morphology shows discrete yellow-white plaques adherent to the colonic mucosa, which histologically consist of a volcano-like eruption of fibrin, inflammatory cells, and necrotic debris. Stevens-Johnson syndrome and its more severe form, toxic epidermal necrolysis, are life-threatening mucocutaneous reactions most commonly triggered by sulfonamides, anticonvulsants such as carbamazepine and phenytoin, and allopurinol; histopathology reveals full-thickness epidermal necrosis with sparse lymphocytic infiltration, and the clinical presentation includes widespread blistering and sloughing of skin and mucous membranes.

Nonsteroidal anti-inflammatory drugs produce gastropathy through inhibition of cyclooxygenase-1, leading to decreased prostaglandin-mediated mucosal protection; endoscopically and pathologically, this manifests as gastric erosions, ulcers, and hemorrhagic gastritis. The same agents cause nephropathy through papillary necrosis and chronic interstitial nephritis. Anticoagulants such as warfarin, heparin, and direct oral anticoagulants cause bleeding complications ranging from minor ecchymoses to fatal intracranial hemorrhage, with pathological findings showing hemorrhage into soft tissues, joints, or body cavities. Corticosteroids produce a wide array of iatrogenic effects including immunosuppression with increased susceptibility to opportunistic infections, osteoporosis with thinning of trabecular bone and increased fracture risk, avascular necrosis particularly of the femoral head, Cushing syndrome with characteristic facial and truncal fat redistribution, and adrenal suppression due to feedback inhibition of the hypothalamic-pituitary-adrenal axis. Opioids cause respiratory depression through suppression of brainstem respiratory centers, as well as constipation due to reduced gastrointestinal motility. Contrast media used in diagnostic imaging may cause contrast-induced nephropathy, characterized by acute tubular injury, and anaphylactic reactions ranging from mild urticaria to life-threatening cardiovascular collapse.

Surgical iatrogenesis and postoperative complications

Surgical interventions produce a distinct set of iatrogenic conditions. Retained foreign bodies, most notably gossypiboma or retained surgical sponge, and less commonly retained surgical instruments, elicit a characteristic foreign body reaction. The morphology of gossypiboma includes a mass of cotton fibers surrounded by either an exudative inflammatory response with abscess formation or an aseptic fibrous reaction with granulomas and foreign body giant cells. Wrong-site surgery represents a preventable medical error with profound consequences for the patient. Anesthetic complications include malignant hyperthermia, a life-threatening hypermetabolic state triggered by volatile anesthetics and succinylcholine in susceptible individuals, characterized by muscle rigidity, hyperthermia, rhabdomyolysis, and hyperkalemia. Awareness during general anesthesia occurs when the patient remains conscious and recalls events during surgery despite apparent unconsciousness. Aspiration of gastric contents during anesthesia leads to chemical pneumonitis, histologically showing diffuse alveolar damage with necrotic debris and inflammatory cells.

Postoperative infections are common iatrogenic complications. Surgical site infections involve the incision or deeper soft tissues and are characterized by suppurative inflammation, abscess formation, and delayed wound healing. Nosocomial pneumonia, including ventilator-associated pneumonia, shows histopathological features of bronchopneumonia with neutrophilic infiltration of alveolar spaces. Catheter-related bloodstream infection and catheter-associated urinary tract infection are device-related iatrogenic conditions that produce bacteremia, pyelonephritis, and septic complications. Thromboembolic complications including deep vein thrombosis and pulmonary embolism arise from the hypercoagulable state induced by surgery, immobilization, and vascular injury; the pathology shows venous thrombi composed of fibrin, red blood cells, and platelets, which may embolize to the pulmonary arteries causing right heart failure and sudden death. Anastomotic leak following gastrointestinal surgery leads to peritonitis, intra-abdominal abscess, and sepsis. Postoperative hemorrhage may result from inadequate hemostasis or vessel injury. Nerve injury during surgery causes denervation atrophy of affected muscles and sensory deficits in the corresponding dermatomes.

Transfusion-related complications

Transfusion of blood products carries multiple iatrogenic risks. Acute hemolytic transfusion reaction occurs from ABO incompatibility, where recipient antibodies destroy donor red blood cells, leading to hemoglobinemia, hemoglobinuria, disseminated intravascular coagulation, and acute renal failure; pathology shows hemoglobin casts in renal tubules and acute tubular necrosis. Febrile non-hemolytic transfusion reaction results from recipient antibodies against donor leukocytes. Allergic transfusion reaction, ranging from urticaria to anaphylaxis, reflects recipient sensitivity to donor plasma proteins. Transfusion-related acute lung injury, or TRALI, is a leading cause of transfusion-associated mortality and presents clinically as acute respiratory distress syndrome within six hours of transfusion; histopathologically, it shows diffuse alveolar damage with

neutrophilic sequestration in the pulmonary microvasculature. Transfusion-associated circulatory overload, or TACO, results from volume overload in susceptible patients, leading to pulmonary edema and cardiac failure. Infectious transmission of viruses such as hepatitis B, hepatitis C, and HIV, though rare in modern blood banking, remains a potential iatrogenic complication.

Radiation-induced iatrogenesis

Therapeutic radiation produces both acute and chronic tissue damage. Acute radiation dermatitis shows histologically as epithelial cell death, inflammatory infiltration, and loss of hair follicles and sweat glands. Long-term radiation injury is characterized by vascular sclerosis with hyalinization of vessel walls, tissue fibrosis with dense collagen deposition, atypical fibroblasts, and loss of regenerative epithelium in organs such as the skin, gastrointestinal tract, and bone marrow. Radiation also carries a risk of secondary malignancies, including sarcomas and carcinomas, arising within the radiation field years after treatment.

Diagnostic errors and medication errors

Diagnostic errors constitute a significant category of iatrogenic pathology. Missed diagnosis occurs when a condition is not identified at all, delayed diagnosis occurs when identification is postponed beyond the appropriate timeframe, and incorrect diagnosis occurs when a patient receives a diagnosis of a disease they do not have. Overdiagnosis refers to the detection of a condition that would never have caused symptoms or harm, leading to unnecessary treatment and anxiety. False-positive test results lead to unnecessary further testing and psychological distress, while false-negative results provide false reassurance and delay appropriate treatment. Medication errors encompass a range of preventable events including administration of the wrong drug, wrong dose, wrong route, wrong patient, wrong time, and omission of a necessary medication. These errors may result from illegible handwriting, similar drug names, miscalculations, or failure to check patient identification.

Psychological iatrogenesis

Beyond physical injury, medical interventions may produce psychological harm. The nocebo effect describes adverse symptoms or worsening of condition induced by negative expectations and beliefs about a treatment, contrasting with the placebo effect. Anxiety may be induced by a frightening diagnosis, by abnormal test results that ultimately prove benign, or by the anticipation of painful procedures. Stigmatization occurs when a medical diagnosis carries social or psychological burdens, such as a diagnosis of mental illness, HIV, or obesity, leading to discrimination, social isolation, and diminished self-esteem.

Morphology of iatrogenic pathology

The morphologic changes in iatrogenic pathology are highly variable and reflect the specific mechanism of injury. Drug-induced liver injury may show hepatocellular necrosis with confluent or zonal patterns, cholestasis with bile plugs

in canaliculi and hepatocytes, or granulomatous inflammation with epithelioid histiocytes. Chemotherapy toxicity produces bone marrow suppression with profound hypocellularity and replacement of hematopoietic elements by fat, gastrointestinal mucosal atrophy with blunted villi and crypt loss, and cardiomyocyte degeneration with vacuolization and myofibrillar loss as seen with doxorubicin. Radiation damage demonstrates vascular sclerosis with thickened hyalinized walls, tissue fibrosis with abundant collagen deposition, atypical fibroblasts with enlarged hyperchromatic nuclei, and loss of regenerative epithelium in affected organs. Surgical trauma yields hemorrhage, necrosis, ischemia-reperfusion injury, and foreign body reactions to suture materials, which histologically show multinucleated giant cells surrounding suture fibers. Histopathological evaluation by the pathologist often reveals features specific to the causative agent or intervention, making the autopsy and biopsy examination essential for recognizing and documenting iatrogenic conditions.

Clinical presentation, complications, and outcomes

Iatrogenic conditions may result in acute complications such as anaphylaxis, hemorrhage, or acute renal failure, or they may lead to chronic disability such as drug-induced Parkinsonism, post-surgical adhesions causing bowel obstruction, or radiation fibrosis restricting organ function. Some complications, including contrast-induced nephropathy and chemotherapy-induced bone marrow suppression, may resolve with supportive care, while others cause irreversible damage such as deafness from aminoglycosides or cardiomyopathy from anthracyclines. Deaths from iatrogenic causes are often multifactorial and include fatal drug reactions such as Stevens-Johnson syndrome or arrhythmias from QT-prolonging agents, postoperative complications including sepsis, thromboembolism, or hemorrhage, device failure or mismanagement such as cardiac arrest from pacemaker malfunction or fatal embolism from central venous catheters, and therapeutic miscalculations such as incorrect dosing of chemotherapeutic agents or insulin leading to fatal toxicity or hypoglycemia.

Prevention strategies

Prevention of iatrogenic pathology requires a multifaceted approach. Checklists, most notably the World Health Organization Surgical Safety Checklist, have been shown to reduce surgical complications and mortality through systematic verification of critical steps. Medication reconciliation involves creating an accurate list of all medications a patient is taking and comparing that list against physician orders to prevent errors of omission, duplication, or interaction. Clinical decision support systems embedded in electronic health records provide real-time alerts for drug-drug interactions, allergies, and inappropriate dosing. Infection control protocols including hand hygiene compliance, isolation precautions for multidrug-resistant organisms, and sterile technique for invasive procedures reduce nosocomial infections. Root cause analysis is a systematic process for identifying the underlying causes of adverse events and developing corrective actions. Adverse event reporting systems encourage voluntary reporting of errors and near misses to facilitate learning

and system improvement. Quality improvement initiatives use data-driven methods to continuously monitor and enhance the safety and effectiveness of healthcare delivery.

The role of the pathologist in recognizing iatrogenic conditions

The pathologist plays an essential role in recognizing and documenting iatrogenic conditions at autopsy and in biopsy specimens. At autopsy, the pathologist may identify unsuspected retained foreign bodies, unrecognized surgical injuries, fatal drug reactions with characteristic organ findings, or complications of medical devices. In biopsy specimens, the pathologist may diagnose drug-induced liver injury, radiation changes, chemotherapy toxicity, or infectious complications of immunosuppression. The pathologist must maintain a high index of suspicion for iatrogenic causes when the clinical history includes recent medical interventions, and the autopsy report or surgical pathology report should clearly document the nature, extent, and likely cause of iatrogenic findings. This documentation serves not only clinical and medicolegal purposes but also provides critical feedback to healthcare systems for quality improvement and prevention of future adverse events.

INFORMATIONAL AND METHODOLOGICAL PART

MAIN LITERATURE

1. Pathomorphology : textbook / ed. by I.V. Sorokina, V.D. Markovskiy, 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.