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INTRPDUCTION TO PATHOLOGY

Dr Ammar c.Al-Rikabi

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Web site : www.kkbc.com.sa

E-mail : kkbc505@kkbc.com.sa

DEFINITION:

- Pathology is the scientific study of disease.
- The ultimate goal of pathology is the identification of the causes of disease, a fundamental objective that leads the way to disease treatment and prevention.

Clinical Pathology

Clinical medicine is based on a longitudinal approach to a patient's illness - the patient's history, the examination and investigation, the diagnosis and the treatment. Clinical pathology is more concerned with a cross-sectional analysis at the level of the disease itself, studied in depth - the cause and mechanism of the disease, and the effects of the disease upon the various organs and systems of the body. These two perspectives are complementary and inseparable: clinical medicine cannot be practised without an understanding of pathology; pathology is meaningless if it is without clinical implications.

Experimental Pathology

Experimental pathology is the observation of the effects of manipulations on experimental systems such as animal models of disease or cell cultures.

Subdivisions of Pathology

Pathology is a vast subject with many ramifications (branches). In practice, however, it can be split into major subdivisions:

- * **Histopathology:** the investigation and diagnosis of disease from the examination of tissues.
- * **Cytopathology:** the investigation and diagnosis of disease from the examination of isolated cells.
- * **Haematology:** the study of disorders of the cellular and coagulable components of blood.
- * **Microbiology:** the study of infectious diseases and the organisms responsible for them.
- * **Immunology:** The study of the specific defense mechanisms of the body.

- * **Chemical pathology:** the study and diagnosis of disease from the chemical changes in tissues and fluids.
- * **Genetics:** the study of abnormal chromosomes and genes.
- * Toxicology: the study of the effects of known or suspected poisons.
- * **Forensic pathology:** the application of pathology to legal purpose (e.g. investigation of death in suspicious circumstances).

TECHNIQUES OF PATHOLOGY

Light microscopy

Advances in the optical quality of lenses have resulted in a wealth of new information about the structure of tissues and cells in health and disease that can be obtained from their examination by light microscopy.

If solid tissues are to be examined by light microscopy, the sample must first be thinly sectioned to permit the transmission of light and to minimize the superimposition of tissue components. These sections are routinely cut from tissue hardened by permeation with and embedding in wax, or less often, transparent plastic. For some purposes (e.g. histochemistry, very urgent

diagnosis) sections have to be cut from tissue that has been hardened rapidly by freezing (frozen section). The sections are stained to help distinguish between different components of the tissue (e.g. nuclei, cytoplasm, collagen).

Immunohistochemistry and immunofluorescence

Immunohistochemistry and immunofluorescence employ antibodies (immunoglobulins with antigen specificity) to visualize substances in tissue sections or cell preparations; these techniques use antibodies linked chemically to enzymes or fluorescence dyes respectively. Immunofluorescence requires a microscope specially modified for ultraviolet illumination and the preparations are often not permanent (they fade). For these reasons, immunohistochemistry has become more popular; in this technique, the end product is a deposit of opaque or colored material that can be seen with a conventional light microscope and does not deteriorate.

Electron Microscopy

Electron microscopy has extended the range of pathology to the study of disorders at the organelles level, and to the demonstration of viruses in tissue samples from some diseases.

Biochemical Techniques

Biochemical techniques applied to the body's tissues and fluids in health and disease are now one of the dominant influences on our growing knowledge of pathological processes. The clinical role of biochemistry is exemplified by the importance of monitoring fluid and electrolyte homeostasis in many disorders. Serum enzyme assays are used to assess the integrity and vitality of various tissues; for example, raised levels of cardiac enzymes in the blood indicate damage to cardiac myocytes.

Haematological Techniques

Haematological techniques are used in the diagnosis and study of blood disorders. These techniques range from relatively simple cell counting, which can be performed electronically, to assays of blood coagulation factors.

Cell Cultures

Cell cultures are widely used in research and diagnosis. They are an attractive medium for research because of the ease with which the cellular environment can be modified and the responses to it monitored (observed). Diagnostically, cell cultures are used to prepare chromosome spreads for cytogenetic analysis.

Medical Microbiology

Medical microbiology is the study of diseases caused by organisms such as bacteria, fungi, viruses and parasites. Techniques used include direct microscopy of appropriately stained material (e.g. pus), culture to isolate and grow the organism and methods to identify correctly the cause of the infection. In the case of bacterial infections, the most appropriate antibiotic can be selected by determining the sensitivity of the organism to a variety of agents.

Molecular Pathology

Many advances are now coming from the relatively new science of molecular pathology, defects in the chemical structure

of molecules arising from errors in the genome, the sequence of bases that directs amino acid synthesis.

GENERAL AND SYSTEMATIC PATHOLOGY

Pathology is best taught and learnt in two stages:

- * **General pathology:** the mechanisms and characteristics of the principal types of disease process (e.g. congenital versus acquired diseases, inflammation, tumours, degeneration).
- * **Systematic pathology:** the descriptions of specific diseases as they affect individual organs or organ systems (e.g. appendicitis, lung cancer, atheroma).

LEARNING PATHOLOGY

There are two apparent difficulties that face the new student of pathology: language and process. Pathology, like most branches of science and medicine, has its own vocabulary of special terms: these need to be learnt and understood not just because they are the language of pathology but because they are also a major part of the language of clinical medicine. The student must not confuse the learning of the language with the learning of the mechanisms of disease and their effects on individual organs

and patients. For example, the term “hyperplasia” means an increase in the size of an organ due to the proliferation of its constituent cells; this definition must be learnt before the student attempts to learn about the process of hyperplasia.

A logical and orderly way of thinking about diseases and their characteristics must be cultivated; for each entity the student should be able to run through the list of chief characteristics that apply to any disease:

- * Incidence.
- * Aetiology.
- * Pathogenesis.
- * Pathological and clinical features.
- * Complication and sequelae.
- * Prognosis.

MAKING DIAGNOSES

Diagnosis is the act of naming a disease in an individual patient. The diagnosis is important because it enables the patient to benefit from treatment that is known, or is at least likely, to be effective from observing its effects on other patients with the same disease.

The process of making diagnosis involves:

- * Taking a clinical history to document symptoms.
- * Examining the patient for clinical signs.
- * If necessary, performing investigations guided by the provisional diagnosis based on signs and symptoms.

Although experienced clinicians can diagnose many patient's diseases quite rapidly (and possibly reliably), the student will find that it is helpful to adopt a formal strategy based on a series of logical steps leading to the gradual exclusion of various possibilities and the emergence of a single diagnosis. For example:

- * First decide which organ or body system is likely to be affected by the disease.
- * From the signs and symptoms, decide which general category of disease (inflammation, tumours, etc) is likely to be present.
- * Then, using other factors (age, gender (sex), previous medical history, etc). compute a diagnosis or a small number of possibilities for investigation.

- * Investigations should be performed only if the outcome of each one can be expected to resolve the diagnosis, or influence management if the diagnosis is already known.

Diagnostic Pathology

In living patients, we investigate and diagnose their illness by applying pathological methods to the examination of tissue biopsies and body fluids.

Biopsies and organ resections

Biopsies are samples of tissue removed from a patient for diagnostic purposes. Resection specimens (e.g. gastrectomies, thyroidectomies) are the whole or part of an organ removed for a previously diagnosed condition: In addition to their diagnostic utility, much is being learned about the pathology of many diseases from the study of these tissue samples.

Biopsies can be obtained by a variety of methods:

- * Needle biopsy: from solid tissues using a thick-bored cutting needle.
- * Endoscopic biopsy: visually-guided biopsy of an internal body surface (e.g. alimentary or respiratory tracts).

- * Incisional biopsy: tissue removed by surgical incision (e.g. wedge biopsy of liver).

Cytology

Cytology involves the examination and interpretation of dispersed cells rather than solid tissues, usually for the diagnosis of cancer and pre-cancerous lesions. These cells can be obtained by a variety of methods according to the organ being investigated:

- * **Exfoliative cytology:** cells shed from, or scraped or brushed off, an epithelial surface (e.g. bronchus, cervix).
- * **Fluid cytology:** cells withdrawn with the fluid in which they are suspended (e.g. peritoneal and pleural effusion, urine).
- * **Washing:** cells flushed out of an organ using an irrigating fluid (e.g. bronchial washings from the lung).
- * **Fine needle aspiration cytology:** cells sucked out of a solid tissue (e.g. breast lump) using a thin needle attached to a syringe.

Blood

Blood is easy to sample by venepuncture; arterial blood is necessary only when gas analyses (e.g. O₂, CO₂) are to be

performed. Many observations and measurements can be made on blood samples; for example:

- * Blood cells: the morphology and concentration in the blood are important in the investigation and diagnosis of anaemias, leukaemias, infections and immune status.
- * Plasma: for the investigation of abnormalities of blood coagulation.
- * Serum: commonly used (because it does not coagulate) for biochemical assays of electrolysis, enzymes, proteins, etc.

Excretion and secretions

Urine and faeces are commonly investigated by microbiological methods in cases of suspected infection of the urinary tract and gastrointestinal tract respectively. In some non-infectious conditions, biochemical analyses (of urine and faeces) are helpful.

Sputum is an important source of diagnostic material in respiratory tract disease. Malignant cells may be shed from the surface of a bronchial tumour and expectorated in the sputum where they can be found by cytological examination. In lower respiratory tract infections (bronchitis and pneumonia), the

causative organisms can often be found in the sputum by microbiological methods.

Effusions and Exudates

Effusions of fluid into body cavities (e.g., peritoneal, pleural) may be due to a variety of causes. Measuring the protein concentration in the fluid may be helpful in distinguishing between different mechanisms by which the fluid might have accumulated. Of greater value, however, is cytological examination of the body fluids for neoplastic cells.

Effusions and exudates (e.g., pus and pathological discharges) may also be provoked by infections. Microbiological examination of the material is vitally important in such cases so that the causative organisms can be identified and the most appropriate treatment prescribed.

AUTOPSIES

Autopsy (necropsy and post-mortem examination are synonymous) means to “see for oneself”. In other words, rather than relying on clinical signs and symptoms and the results of diagnostic investigations during life, here is an opportunity for direct inspection and analysis of the organs.

Autopsies are useful for:

- * Determining the cause of death.
- * Audit (assess or check) the accuracy of clinical diagnosis.
- * Education of undergraduates and postgraduates.
- * Research into the causes and mechanisms of disease.
- * Gathering accurate statistics about disease incidence.