What is Pathology?
An Overview

Dr Ben Dessauvagie
Ben.Dessauvagie@health.wa.gov.au
UWA Adjunct Senior Lecturer
FSH Consultant Anatomical Pathologist
Objectives

• become familiar with the pathological basis of disease
• learn about the different disciplines of pathology and the role they play in contributing to the diagnosis, stratification and monitoring of human disease
What is Pathology?

- Pathos
  - ‘suffering’
- Logia
  - ‘to study’

- The study of the nature and cause of human disease
What is Pathology?

• Medical specialty concerned with the study of the nature and causes of diseases

• Pathology underpins all aspects of medicine
  • Investigating the causes of disease
  • Analysis of blood, body fluids and tissues
  • Making a diagnosis
  • Role in disease prevention
  • Monitoring and guiding treatment (inc blood transfusions)
  • Medical research
  • Determining the cause of death
What is Pathology?
What is Pathology?

- Pathology is integral to the diagnosis of the majority of diseases
  - 70% of treatment decisions rely on pathology results
  - 100% of cancers diagnosed by pathology
- In Australia
  - 1 in 2 have a pathology test every year
  - 100 tests per minute in Australia
- Affects every stage of life
  - Pre-conception
  - Throughout gestation
  - Growth, development, ageing and death
What is Pathology?

• Some important pathology definitions...

• Disease: an abnormal condition that affects the body of an organism
• Aetiology: the cause of a disease or condition
• Pathogenesis: manner of development of a disease
Aetiology

• Inherited/congenital
• Acquired
  • Infectious agents
  • Trauma
  • Vasculature events
  • Immune reactions
  • Metabolic disorders
  • Nutrition and the environment
  • Idiopathic
  • Neoplasia
Pathogenesis

• The cellular events, changes and reactions instigated by the aetiology that alter normal cellular processes

• Examples of pathogenesis:
  • Inflammation and pus formation
  • Necrosis (cellular +/- tissue death)
  • Neoplasia (malignant change – cancer)
  • etc
Alcohol

Gas permeability
Endotoxemia
Kupffer cell activation
Inflammation

ADH
Acetaldehyde
Stellate cell activation
Hepatocyte injury

CYP2E1
Oxidant stress
PDGF, TGF-β
Fibrosis

Malnutrition
Impaired regeneration
Alcoholic hepatitis

Source: J Gastroenterol Hepatol © 2003 Blackwell Publishing
Recognising Pathology

• Levels of examination:
  • Macroscopic
  • Microscopic
  • Ultrastructural
  • Genetic
  • Functional
Recognising Pathology

• Macroscopic
  • Grossly appreciable structural manifestations of disease
  • Recognised at clinical exam, radiologically or by gross examination in the laboratory/mortuary
Recognising Pathology

• Macroscopic
Recognising Pathology

• Microscopic
  • Microscopic manifestations of disease
  • Recognised by examination with the light microscope
Recognising Pathology

• Ultrastructural
  • Manifestations of disease at subcellular level (e.g. cellular organelles, matrix proteins)
  • Recognised by examination with the electron microscope
Recognising Pathology

• Genetic
  • Examination of the chromosomal, molecular and nucleic acid abnormalities in disease.
  • Recognised by “genetic tests”. Technology rapidly advancing.
  • E.g. Sanger Sequence, Karyotype, FISH, NGS
Recognising Pathology

• Functional
  • Detect aberrant cellular functions (pathophysiology) as the cause or result of disease
  • Recognised by variety of tests, particularly biochemical & haematological

<table>
<thead>
<tr>
<th>Test</th>
<th>Patient</th>
<th>Reference Range</th>
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<tbody>
<tr>
<td>PT</td>
<td>13s</td>
<td>11-14s</td>
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<tr>
<td>APTT</td>
<td>105s</td>
<td>23-35s</td>
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<td>Fibrinogen (Clauss)</td>
<td>2.7g/L</td>
<td>1.5-4.0g/L</td>
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<tr>
<td>Thrombin Time</td>
<td>13s</td>
<td>10-13s</td>
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Pathology and the Patient

• Symptoms: things the patient feels
  • A departure from normal function or feeling
  • Noticed by the patient
  • E.g. Hot, cold, lump, rash, weight loss, tired, lethargic

• Signs: physical findings
  • Objective evidence of disease
  • Noticed by doctor on clinical examination
  • E.g. Temperature, mass, type of rash, heart rate, resp rate, enlarged organs

• Investigations:
  • Pathology & radiology
Pathology Tests

• Pre-analytic
• Specimen received with request form
  • Patient details
  • Specimen details
  • Clinical information
  • Requesting doctor
  • Correct specimen preparation (e.g. patient fasted, correct fixative, correct timing)
Pathology Tests

• Analytic/Testing Phase
• Samples processed and results obtained
• Accuracy and reproducibility ensured by internal and external quality assurance
  • Positive and negative controls
  • Internal audit
  • External QAP
  • External accreditation
Pathology Tests

- Post analytic phase
- Pathologist/Scientist validates results
- Report issued to requesting doctor in a timely fashion
Disciplines of Pathology

- Anatomical pathology
  - Histopathology
  - Cytopathology
- Chemical pathology
- Haematology
- Genetic pathology
- Immunology
- Microbiology
- Forensic pathology
Anatomical Pathology

• The morphologic examination of tissues and cells to diagnose and study the manifestations of disease

• Two subspecialties
  • Histopathology: the examination of a biopsy or surgical specimen by a pathologist for a tissue diagnosis.
  • Cytology: the examination of cellular elements either in fluids (e.g. urine), brushed from a surface (e.g. pap smear) or aspirated from a lump (fine needle aspiration)
The anatomical pathologist

- Macroscopic tissue assessment
- Tissue processing and slide preparation
- Routine stains (Haematoxylin & Eosin/Papanicolaou)
- Microscopic review
- Special stains (Immunohistochemistry, micro-organisms, etc.)
- Genetic analysis
- Interpretation in clinical/radiological context
- Liaising with clinicians
- Laboratory supervision
Chemical Pathology

• Detecting changes in a wide range of substances in blood and body fluids to diagnose and manage disease
  • Electrolytes, fats, sugars, enzymes and proteins
  • Hormones, vitamins and minerals
  • Tumour (cancer) markers
  • Poisons and both therapeutic and illicit drugs
The Biochemist

- Review and interpretation of abnormal tests in clinical context
- Recommend management to clinicians
- Laboratory supervision
Haematology

- The examination of blood and bone marrow to diagnose and manage disease
  - Blood counts
  - Bone marrow examination
  - Coagulation and bleeding disorders
  - Blood transfusion
The Haematologist

• Interpretation of blood, bone marrow and clotting tests
• Integrate results in clinical context
• Recommend management to clinicians
• Advise on blood transfusion:
  • Indicated or not; alternatives and risks
  • Ensures blood products are used appropriately
• Laboratory supervision
Microbiology

• Diagnosis and treatment of disease caused by infections
• Examination of tissue/fluid/other collected by a wide variety of methods and procedures
• Bacterial, viral, fungal, protozoal
• Determining appropriate anti-microbial therapy
The Microbiologist

- Diagnoses infectious diseases based on:
  - Cultured microorganisms
  - Serological testing
  - Molecular biology: PCR, sequencing
- Advises clinicians about treatment
- Public Health role
- Laboratory supervision
Immunology

- Diagnosis and monitoring of diseases which affect the immune system
  - Immunodeficiency: Underactivity of the immune system
  - Autoimmunity: Misdirected activity of the immune system against the patient’s own tissues
  - Allergy: Overactivity of the immune system to substances (allergens) innocuous to most people
The Immunologist

- Diagnosis, treatment and monitoring of immune related diseases
- Interprets results of serology, allergy and immunofluorescence tests in clinical context
- Prescription of immunomodulatory drugs to boost or dampen immune system
- Determine allergens/precipitants and instigate sensitisation to prevent allergic reactions
- Laboratory supervision
Genetic Pathology

• Diagnosis of disease with an inherited or acquired genetic aetiology

• Assess abnormalities in chromosomes and DNA to help diagnose disease
  • Chromosomes: Cytogenetics, FISH
  • DNA: Sanger sequencing, NGS
The Genetic Pathologist

• Diagnosis of inherited or congenital diseases
• Advise clinicians on whether to test for a genetic abnormality
• Advise clinicians on risk and prediction, esp in prenatal setting
• Genetic counselling: results have implications for families
• Increasing involvement with genetics of cancer
• Laboratory supervision
Forensic Pathology

• Primarily concerned with determining the cause of death at the request of the coroner
  • Sudden, unexpected death
  • Unnatural violent death
  • Death in custody
  • Suspicious death

• Principle method of investigation is autopsy
• Also – radiology, biochemistry, microbiology, haematology
The Forensic Pathologist

• Performs autopsies
• Takes samples of tissues, blood and fluid for ancillary tests
• Synthesises pathology findings with available history
• Provides report to coroner. May have disease prevention/public health implications
• Provides evidence in court
• Victim identification in natural disasters/mass killings
  • DNA, toxicology
  • Anthropology
  • Dental records
• Laboratory supervision
Take home messages

• Pathology is a broad medical specialty studying the nature and cause of disease
• Aetiology and pathogenesis are the pathological basis of disease
• Pathology manifests as structural and functional abnormalities which can be recognised by pathology test
• Quality control is imperative for accuracy and reproducibility
• Seven disciplines each with a role in diagnosis, treatment and monitoring of human disease
What is Pathology?

https://www.rcpa.edu.au/Pathology-Careers/What-is-Pathology