History of Pathology

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Outline

• The beginnings of pathology
• Early understanding of the body
• Normal body structure and function
• Autopsies and disease
• Microbes and man
• Early blood transfusion
• Modern pathology
Milestones in History of Pathology

• BC: Egyptians and Greeks
• 1st century AD: Galen
• 15th century: Benivieni: autopsies
• 16th century: Vesalius: anatomy
• 17th century: Harvey: blood & transfusion
• 18th century: Morgagni & Hunter
• 18th century: Cancer & microbes
• Mid 19th century: Microscope, stains
• 20th century: Cytochemistry; EM; IHC; genes
2500BC – 999 CE “Mirror of the Soul”

• The body: a mystery to the world of science
• Different cultures employed various forms of observation, experience, ritual, intuition, and other methods to combat illness
• Varying degrees of success
• Exploration of human physiology was elusive
• No understanding of tissue or blood
Ancient Egypt

• Egyptian medicine:
  – 1st documentation of disease
  – 17 century BC Edwin Smith papyrus: different types of bone injuries, ulcerating “lumps”
  – Mummies: bone tumours, gall stones, abscesses
  – No knowledge of the underlying processes
  – **Gods were the cause of disease**
  – Cancer: tumour against god Xenus
2500 – 400 BC

• C 2500 BC: Egyptians used bleeding to treat patients

• C 500BC: Arteries and veins were noted to be different (from animal dissection)

• C 450 – 400BC Empedocles (Greek philosopher):
  – Believed the heart to be the organ of sense
  – Theorised that all matter is comprised of four "roots“: earth, fire, air, water
Hippocrates of Kos

• Greek physician (460 – c370BC)
• Father of Western medicine
• Rejected idea of disease as affliction of gods
• Body composed of 4 humours (‘humourism’)
  – Blood: sanguine
  – Phlegm: phlegmatic
  – Yellow bile: choleric
  – Black bile: melancholic
• Imbalance of the humours was the cause of disease
350 BC - AD

• C 350 BC: Aristotle:
  – Believed the heart to be the central organ of the body and the seat of the soul.
  – Conducted animal dissections and described anatomical structures

• Cornelius Celsus:
  – Roman encyclopaedist (30BC – 38AD)
  – Classic definition of inflammation
  – *rubor* (redness), *tumour* (swelling), *calor* (warmth), *dolor* (pain)
Claudius Galen (b.130AD)

- Most significant Roman physician
- Followed Hippocratic concepts of 4 humours
- Prodigious writings on pathology
- Extensive animal dissections formed the basis for his theories and teachings
- Proved that arteries contain blood
- Many false theories
- But, *ideas persisted for 15 centuries*
1000 – 1699 “Status Quo Under Fire”

• Mid 1200s: Cairo physician Ibn al-Nafis discovered & described pulmonary circulation

• Preserved and translated the Greek writings

• Had an awareness of Indian medicine

• Translations in Spain passed this knowledge to Europe

• *Did not progress understandings of disease*
European Renaissance Period

• Antonio Benivieni (1443-1502)
  – Florentine physician who pioneered the use of the autopsies to understand the cause of death
  – Published *De Abditis Morborum Causis* ("The Hidden Causes of Disease"): one of the first pathology works

• 16th and 17th century:
  – Anatomists
  – Were aware of pathological structures as a result of their anatomical studies
  – Andreas Vesalius 1514-1564 (b. Brussels)
Andreas Vesalius (1555)

- On graduation appointed to Chair of Surgery and Anatomy at Padua
- Studied Galen’s works on animal dissection and challenged and disproved some of his ideas
- Dissected bodies of executed criminals
- Hands-on direct observation of the body
- Published work on findings from human autopsies: “the anatomical view of the body”, one of the earliest anatomy books

- **Founder of modern human anatomy**
The Seventeenth Century

- Harvey: Circulation of blood, 1613
- 17th Century - a haphazard mixture of:
  - Folk cures, astrology, religion
  - Lessons from the Greek
- Treatments included:
  - Roots, worms, herbs
  - Powders from crabs eyes, viper’s tongues
- Barbers operated as frequently as surgeons
- Bleak times, but also time of innovation
William Harvey (1578 – 1657)

• English physician
• Revolutionised concepts of disease causation
• A severe blow to the humoural theory
• 1613: Described circulation of the blood through the pumping of the heart
• Observed cardiac pathology:
  – Ventricular rupture
Jean-Baptiste Denis 1667

- Physician to Louis XIV
- Gave the first reported blood transfusion to Antoine Mauroy, a madman
- Direct transfusion of calf blood
- Beginnings of blood transfusion
The French Response

- Two of first four transfusion recipients died
- French physicians disapproved
- April 17, 1668, French courts determined:
  “that for the future no transfusion should be made upon any human body but by the approbation of the Physicians of the Parisian Faculty.”
- Within ten years transfusion was prohibited in France and England
James Blundell (1790 - 1877)

• Resuscitated transfusion
• London physician
• Troubled by frequency of post-partum haemorrhage “...the patient might very probably have been saved by transfusion.”
• Used human blood to replace blood lost
• Established rational indications for blood transfusion
John Hunter (1728 – 1793)

• Scottish Surgeon

• Initially worked in anatomy with aptitude in dissection and preparation of specimens

• Emphasised the importance of relationship between structure and function

• Advocate of careful observation and scientific method in medicine

• Hunterian Museum, RCS
Percivall Pott (1714-1788) and Chimney Sweepers’ Cancer of the Scrotum

JOHN R. BROWN and JOHN L. THORNTON

From the Department of Applied Physiology, London School of Hygiene and Tropical Medicine, and the Medical College Library, St. Bartholomew’s Hospital, London

With the possible exception of John Hunter, Percivall Pott is remembered as the most eminent surgical writer of his period, and the premier position he held in his profession was recognized not only in England but abroad. The fact that he is associated eponymously with several conditions has ensured that his name is still constantly before the medical profession but the facts of his career are little appreciated. Percivall Pott has not been the subject of a full-scale biography, and there are certain divergencies of opinion among those who have written about him. However, the following brief facts outline the activities of one who published the first description of an occupational cancer, and who should be numbered among the pioneers of occupational medicine.

Born in 1714 in Threadneedle Street, London, on the present site of the Bank of England, Percivall Pott was educated with a view to his becoming a clergyman.
18th Century

- Autopsies more common
- Pathological observations
- Giovanni Battista Morgagni
  - Italian anatomist (1682 – 1771)
  - Beginning of modern medicine and pathology
  - Correlated symptoms with autopsy findings
  - *Diseases had an anatomical and organ basis*
Edward Jenner (1749-1823)

• English physician & surgeon under John Hunter
• Pioneer of smallpox vaccine
• “Father of Immunology”
• “Saved more lives than any other man”
• Milkmaids generally immune to smallpox:
  – Postulated pus in blisters milkmaids received from cowpox protected them from smallpox
  – Infection with cowpox gave immunity to smallpox
• 1796 first smallpox vaccine
Other Milestones in Microbiology

• 1850 Semmelweis
  – Washing hands to stop the spread of disease

• 1862 Louis Pasteur
  – Germ Theory of Disease

• 1867 Joseph Lister:
  – Practised antiseptic surgery

• 1876 Robert Koch:
  – Causal relationship between microbe and disease
  – Nobel Prize 1905 "for his investigations and discoveries in relation to tuberculosis"
19th Century: Microscope Era

- New technology: Optics and the microscope
- Recognition of cells
The Development of the Microscope

Culpeper's Microscope (circa 1730)

Schmidt & Haensch Compound Monocular Microscope (circa 1879)

Nature Through Microscope and Camera. R. Kerr and A.E. Smith. 1905
Evolution of Pathology

• Carl von Rokitansky (1804 - 1878)
  – Championed use of autopsy in studying disease
  – Reputed to have performed 30,000 postmortem examinations in Vienna
  – Chemistry of the blood and disease
  – Teaching of medicine changed to science rather than tradition
Rudolf Virchow (1821 – 1902)

• “Greatest figure in history of pathology”

• Used the microscope for tissue analysis from autopsies

• Initiated the idea that changes in diseased states can be traced to alterations in cells

• *The ‘father’ of cellular pathology*

• Pathology emerged as a separate academic discipline in 2\textsuperscript{nd} half of the C19
History of Leukaemia

• 1845 Rudolf Virchow: large number of white blood cells in blood of a patient: Leukämie

• 1845 John Hughes Bennett (Edinburgh)

• Greek “leukos” “heima“ = white blood”

• 1900 leukemia a family of diseases

• 1913 four types: chronic lymphocytic, chronic myelogenous, acute lymphocytic and erythroleukaemia
Paul Ehrlich (1854-1915)

- “Father of haematology”
- 1878 Doctoral thesis: compared textile dyes and cell staining
- Haematoxylin: 1865
Karl Landsteiner (1868 - 1943)

- Discovered blood groups A, B and C (O)
- Institute of Pathological Anatomy, Vienna
- Agglutination of blood when mixed with others
  - Sera agglutinated red cells of some individuals
- Published 1901: documented cellular differences
- Nobel Prize 1930
History of Blood Transfusion

1628 ○ William Harvey discovers the circulation of blood.

1652 ○ Very first (unsuccessful) transfusion attempt between two chickens.

1665 ○ First successful blood transfusion (which was on a dog), by English physician Richard Lower.

1667 ○ Transfusion of lamb’s blood into an ill 15-year-old boy.

1818 ○ The first successful transfusion of human blood performed by British obstetrician James Blundell.

1901 ○ Three main blood groups (now known as A, B, and O) discovered by Austrian physician Karl Landsteiner (whose birthday we celebrate on World Blood Donor Day on June 14).

1916 ○ Citrate glucose solution prevents blood from coagulating. Blood can now be stored for several days between donation and transfusion.

1929 ○ Australia’s first blood transfusion service founded in Victoria. Dr Lucy Bryce is the honorary Director and undertakes the blood testing.

1937 ○ Levine and Stetson discover the rhesus blood group system and link it to haemolytic disease of the newborn.

1939 ○ Harvard University’s Edwin Cohn invents a way of separating plasma’s various proteins including serum albumin, which he uses to treat shock in wounded soldiers.

1940 ○ The US government establishes a nationwide blood collection program.

1948 ○ Australia’s first mobile donation unit makes its maiden journey to Donnybrook in Western Australia, in a specially equipped train coach.

1960 ○ The first plastic blood packs are used in Australia. Glass bottles are completely replaced by plastic in the 1970s.

1967 ○ The RhD immunoglobulin program is introduced, harvesting anti-Rh antibodies from donor plasma to prevent Rh negative women developing antibodies against their Rh positive babies (this program celebrates its 50th anniversary this year, having saved thousands of babies).

1970 ○ Hepatitis B screening introduced in Australia.

1974 ○ Sydney is one of the first blood centres to mix citrate phosphate dextrose solution with adenine, to allow storage of whole blood for up to five weeks.

1985 ○ The first HIV blood-screening test is licensed and implemented by blood banks, including Australia.

1990 ○ Screening for Hepatitis C is introduced.

Source: Alison Gould and Shereen Tan / Australian Red Cross Blood Service
Cytochemistry (1950s)

- The introduction of science
- Detection & localisation of specific cell components

Gomori trichrome

3. Sudan Black B Stain.
4. Peroxidase Reaction
5. Coarse PAS Positivity with blocks in Lymphoblastic Leukemia.

(From Hayhoe 1960 “Leukemia: Research and Clinical Practice” — Churchill).
19th and 20th Centuries

• End 19th century- era of experimental medicine and pathology

• 20th century - electron microscopy

• Mid-20th century (1953 on) – discovery of double stranded DNA; monoclonal antibodies, cytogenetics

• 21st Century: molecular biology (genomics)
Modern History of Pathology

• Modern tissue and cell processing
• Electron microscopy
• Cell immunology 1980s
  – Monoclonal antibodies
  – Immunocytochemistry
  – Flow cytometry
• Cell genetics 1990s
  – Cytogenetics; karyotype; FISH
• DNA, RNA and molecular biology 2000s
Summary

• History of pathology spans 4,000 years
• Human and technological progress
• Gods and beliefs
• Four humours and theories
• Autopsy – anatomy – pathology
• Microscopy and stains
• Organ-based disease
• Organ – tissue – cell – gene – molecule