### **Tuberculosis and other respiratory disorders**

A brief history

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#### Introduction

- A vast topic; only an introduction (luckily, not very much of importance happened between 500 BCE and 1500 CE!)
- For centuries 'lung disease' consisted of pulmonary tuberculosis ('consumption') and 'the rest'
- Asthma, coughs and colds, empyema recognised in antiquity; hay fever (due to roses) first described ca 900 CE by Al-Rhazi. Lung cancers rare before tobacco smoking became common, and life expectancy sufficient for it to develop

Lung fibrosis, sarcoidosis, emphysema, pneumoconiosis, cystic fibrosis, pulmonary hypertension etc not recognised before the development of diagnostic apparatus and methods such as the microscope, stethoscope, bronchoscope, thoracoscope; pathology, spirometry, bacteriology, radiology

# Antiquity(1)



- Egypt Ebers papyrus describes inhalation of smoke from Henbane placed on heated stones (1550 B.C.)
- China Ma Huang (Ephedra) taken for breathing disorders
- India Ayurvedic tradition. Datura leaves smoked for asthma 600BCE or earlier
- Greece Hippocrates (460-370 BCE) first described clubbing, recognised that empyema required drainage, designed first inhaler
  - Rome Galen (129-201 CE) influenced medical thinking until the 1700s and later. Imbalance of 'Humours' caused disease, 'Doctrine of signatures' could indicate a treatment



- Islam Al-Rhazi (ca 866-925 CE) described Hay Fever ('rose cold') and discussed asthma. Ibn Sina mused on the contagious nature of TB.
- Jewish tradition Maimonides' 'Book on asthma' (1190) advocated chicken soup
- Dark Ages/Medieval period treatments based on herbal medicines & prayer, blood-letting a panacea. Paracelsus (ca. 1520s) studied lung disease in miners
- Horn of Africa frankincense used for treatment of chest infections
- Americas Native Americans smoked dried leaves of tobacco and Lobelia for lung disorders, particularly asthma. Lobelia flowers were used in a tea for coughs and colds.



### **Tuberculosis – a brief review**

Caused by infection with a bacillus (Mycobacterium tuberculosis)
 – related to leprosy

- Ancient disease of man, probably originated from cattle
- One-third of world population is infected only a minority develop disease (lifetime risk about 10%)

Can affect any organ in the body, most commonly the lungs. Gastrointestinal infection due to unpasteurised milk (M bovis); blood-borne spread causes TB in other organs e.g TB meningitis. TB of neck lymph-nodes known as 'Scrofula'

# **Tuberculosis in antiquity**

- TB bacilli isolated from mummies in Egypt ( ca 1000 BCE) & Peru (ca 700-1000 CE). Evidence for spinal TB in both regions
- PTB recognised as 'phthisis' in ancient Greece, 'consumption' in the Bible. PTB almost certainly described in texts from China & India 2000-3000 BCE
- Sylvius (1679) recognised that TB caused consistent changes in organs and tissues
- But prior to development of pathology & bacteriology TB of different organs not generally recognised as same disease



### Scrofula – lymph node tuberculosis



- Scrofula (the 'King's Evil') was thought to be cured by the 'Royal Touch' from 496 CE (Clovis);
   Queen Anne last UK monarch to do so
- Roots of Figwort were used from medieval times to 18thC to treat lymph-node TB (doctrine of signatures)
- Common condition; King Charles Il touched 92,000 people 1662-82

# **Diagnosis before bacteriology & radiology available**



- Auenbrugger described percussion in 1761
- Laënnec invented the stethoscope in 1816
- These 2 discoveries permitted diagnosis of pleural effusions, consolidation, and lung cavities
- Laënnec himself died from TB in 1826



### **Consumption – the Romantic Disease**

By early 19thC PTB came to have romantic associations, dying heroines were depicted in opera, many young poets, authors, artists died from TB (Chopin, Keats, the Brontës, Beardsley...)

Concept of 'spes phthisica' – TB could enhance hopefulness & creativity (Keats was told his condition was due to 'too great excitement of poetry')

Contributed to vampire myth in New England

 In reality there was no effective treatment, patients suffered with fever, sweats, bloodstained cough, & died; or were often left breathless



# **TB treatment in the pre-antibiotic era**

- Laennec (1810) mentions inhalations of balsam, myrrh, and aromatics for TB; creosote, eucalyptus, also used. Later, iodine vapour
- 19th & early 20thC era of 'quack cures' electrotherapy, Umckaloabo, Spahlinger treatment, Dr Alabone's therapy, Congreve's Balsamic Elixir, Pulmonol, Duket's serum, Crimson Cross cure, Brompton consumption & cough specific, etc
- Tar inhalations, gold, ineffective; heliotherapy & cod-liver oil beneficial (Vit D activates macrophages)
- Blood-letting also potentially beneficial (mycobacteria need iron to grow)
  - Rest and isolation in sanatoria



# **The Sanatorium**





- Sanatoria instituted mid-19thC segregation, bed-rest, fresh air, graded exercise, nutritious food
- 'No spitting' patients had personal sputum pots
- Authoritarian régime dismissal for offences such as visiting the pub



### **Advances in TB**

- 1882 Koch discovers M.tuberculosis, demonstrates it causes TB
- X-rays discovered 1895, 1<sup>st</sup> chest radiograph 1897
- Tuberculin skin testing 1907
- ♦ BCG vaccine introduced 1922
- Collapse therapy' developed 1920s
- First effective antibiotics, streptomycin and PAS, introduced 1940s, followed by isoniazid in 1950
- Shown 1959 that patients do as well on treatment at home as in sanatorium



# **History of lung surgery**

- Hippocrates (4thC BBCE) advocated surgical drainage of empyema
- Hooke (1667) showed that a dog could be kept alive with multiple pleural perforations if ventilated via the trachea
- Drainage of lung abscesses, bronchiectatic and tuberculous cavities was extent of pulmonary surgery until 1880
- 1880s sporadic reports of lung surgery, using anaesthesia and Lister's antisepsis; mainly unsuccessful
- 1904 Sauerbruch operated in negative-pressure cabinet to prevent lung collapse; 1910 intratracheal insufflation introduced; not widely accepted until 1918
- 1931 first successful pneumonectomy



#### **20thC developments: disease recognition**

- von Neergard (1929), Pattle (1955), Clements (1956/7) described lung surfactant system; Avery & Mead (1959) showed infant RDS due to surfactant deficiency
- 1963 genetic A1-AT deficiency shown to be rare cause of emphysema
- Doll & Bradford (1964) showed smoking causes lung cancer. Also recognised (with air pollution) as cause of COPD
- Obstructive Sleep Apnoea recognised, treated with CPAP 1980
- Cystic fibrosis shown to be due to gene variants 1989
- Pulmonary arterial hypertension described, treated with vasodilators in 1980s
- Ciliary disorders shown to be rare cause of bronchiectasis
- Greater recognition of industrial lung disease (coal-miners' lung, asbestos, silica); compensation, protective masks
- Novel viral infections Hantavirus, SARS, MERS; now COVID-19 (Sars-Cov2)

#### 20thC – new methods and techniques

#### Iron lung (polio)1929, PPV 1959

- Novel antibiotics (TB and other), antivirals, & vaccines
- Body plethysmograph 1956
- Measurement of Arterial pH, O<sub>2</sub>, CO<sub>2</sub> in 1960s, subsequently pulse oximeter
- New imaging techniques: CT scanning invented by Hounsfield, 1972; HRCT 1989; gamma scans, PET, ultrasound
  - Pulmonary rehabilitation 1985
  - Lung transplants, gene therapy



# **TB** epidemiology in the 19<sup>th</sup> and 20<sup>th</sup> centuries

- Incidence<sup>↑</sup> due to overcrowding, malnutrition,
  ↓Vit D industrial revolution; TB exported from Europe to colonies
- In 1821 1 in 3 of all deaths in London were due to TB
- Decline in incidence and mortality since 1900 almost independent of the introduction of BCG vaccination in 1922, and effective chemotherapy being introduced in 1944 (streptomycin), 1946 (PAS) and 1951 (isoniazid). Soon appreciated that monotherapy led to development of resistance
- ♦ 5 Million deaths worldwide 1950
- ♦ TB re-imported from ex-colonies
- 4300 new cases in UK 2021



# **20thC: taking eyes off the ball**

- In developed countries TB considered
  'conquered' TB funding, facilities cut
- TB: *î*incidence –due to immunosuppression by HIV, transplants, ageing, alcohol, drugs, medication (anti-TNF); emergence of resistance (MDR, XDR)
- Competition for funds from novel viral infections – COVID-19, avian influenza, Zika, Ebola
- Global eradication timetable put back years by COVID-19



# The End

### **Questions?**

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#### **Beginnings of cardiopulmonary physiology(1)**

- Hippocrates (460-370 BCE) reported frequency & amplitude of breathing
- Galen (129-201 CE) described effects of pneumothorax and cutting intercostal & phrenic nerves, in animals
- Leonardo da Vinci (1452-1519) described residual volume after complete exhalation
- Colombo (1515-59) established concept of pulmonary circulation; Harvey described systemic circulation 1628; Malpighi used compound microscope to discover lung alveoli and capillaries in 1661
- Boyle (1627-91) built an air pump, showed air was necessary for life
- Rev Stephen Hales researched on 'chemistry of the air', measured a maximal expiration, 1727-33
- Lavoisier (1743-94) was first to measure O<sub>2</sub> consumption and CO<sub>2</sub> production at rest and at work
- Abernethy (1793) collected expired air over mercury, assessed vital capacity (VC) at 3150ml

### **B**eginnings of cardiopulmonary physiology(2)

 Beddoes' Pneumatic Institute (1790s) measured lung volumes, but more interested in treatment (with nitrous oxide and other gases)

Davy measured his VC & TV, & RV using an H<sub>2</sub> dilution method

- Menzies (1796) measured TV by immersing subject in a waterfilled barrel up to the neck
- Hutchison devised a water spirometer in 1844, reported VC of >4000 subjects in 1852





# **Therapeutic uses of smoking**

- When introduced to Europe, smoking was perceived as beneficial (despite detractors e.g King James 1's 'Counterblaste to tobacco')
- Still considered 'manly' into 20thC
- Various other substances (e.g stramonium, cannabis, camphor, foxglove, arsenic), were mixed with tobacco

