



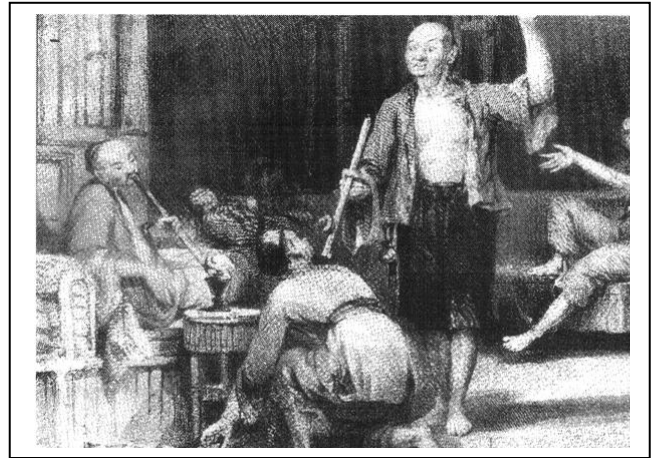
The evolution of Pharmacy, Theme C, level 1

The development of medicines

The origins of medicines

The first drugs probably arose from observation that certain plants had effects other than satisfying hunger and observation has always been the most important tool in the development of medicines.

The oldest drug still in use for its original purpose is opium, which was imported from China where it was known as a sedative and relaxant. In the west it came to be recognised as an analgesic. In ancient times treatments were intended to relieve the symptoms observed. Understanding of the underlying causes of disease was rare.



Early discoveries emerging from science

Throughout the next millennium many drugs were used as laxatives and diuretics but careful observation of their action led to refinement in their use. The most well known is the use of digitalis, by William Withering, for the relief of dropsy in 1785; later recognised as treating the underlying heart failure. It took much longer for the observation that citrus fruits prevented scurvy in sailors on long voyages by James Lind in 1747 to lead to the isolation of ascorbic acid and the recognition of vitamins as essential to nutrition in the 1930s.

Two discoveries led to rapid expansion of surgery from the battlefield into the hospital: antiseptics and anaesthetics. The introduction of phenolic compounds as antiseptics by Joseph Lister in the 1860s allowed surgery on internal organs. The discovery of the properties of nitrous oxide and chloroform to render a patient temporarily unconscious allowed longer operative procedures to be undertaken. Resistance to the use of the new anaesthetics was greatly reduced when chloroform was used during childbirth by Queen Victoria.

The impact of bacteriology

It was not until the nineteenth century that a more logical approach to drug development was established and from then on it runs in parallel with discoveries in other medically related disciplines. The science of bacteriology grew rapidly and the role of micro-organisms in fermentation and disease was postulated. This linked to the work of Edward Jenner (1798) on

the prevention of smallpox which led to laboratories being established all over Europe to search for vaccines in the hope of both preventing epidemics and treating established disease.

Another bacteriologist Paul Erlich, working on the selective staining of bacteria for identification purposes produced the first chemotherapeutic agent, arsphenamine, (also known as “*Magic Bullet 606*”) against syphilis in 1910. Chemical manufacturers now began to test synthetic chemicals, especially from the dye industry, against particular organisms in infected animals and became pharmaceutical companies as a result. Bayer successfully developed the dye prontosil red, active against streptococcal infections. This was soon shown to be the pro-drug of sulphanilamide which was the first successful treatment for pneumonia and saved many lives. Perhaps the most famous instance of discovery following chance observation also occurred in the field of bacteriology; Alexander Fleming’s discovery of penicillin in 1928. The development of penicillin as a commercial product was expedited by the war-time collaboration of the pharmaceutical industry in the UK and USA as was the search for other active substances produced by living organisms grouped together as antibiotics. One of the most important discoveries from soil-based organisms was streptomycin by S A Waksman (1944) active against tuberculosis’ another major killer diseases of the nineteenth and early twentieth centuries. Unfortunately resistance soon built up to the early antibiotics and the pharmaceutical industry began to search for synthetic modifications to combat this and increase stability to allow oral administration.

Impact of physiology and pharmacology

The development of physiology, particularly the identification of glands whose hormone secretions were active throughout the body, was another starting point for drug development. The isolation and analysis of the secretions led first to replacement therapy with thyroid extracts (1890s) and insulin (1923) and later to more reliable therapy with synthetically produced material. The identification of various steroid molecules followed with cortisone in 1948 and the sex hormones in 1955 resulting in the first field studies of the contraceptive pill in 1960. In the second half of the twentieth century emphasis was again given to the relief of symptoms but this time with the support of science. Pharmacology was beginning to establish the mechanisms by which symptoms were produced even where the cause of the malfunction was still unknown.

The therapeutic revolution of the 1950s & 1960s

Keen observation during pharmacological studies often revealed unexpected effects. The action of an antihistamine promethazine observed on the central nervous system led to the development of the antipsychotic phenothiazines. The introduction in 1950 of chlorpromazine was a milestone in the treatment of mental illness and was largely responsible for the disappearance of the strait-jacket and locked wards.



Pharmacological screening of chemicals with similar structures led to the discovery of the tricyclic antidepressants. Isoniazid, originally introduced in 1952 as a competitive antagonist in the treatment of tuberculosis to reduce the development of resistance to streptomycin, was found to have an effect on enzymes in the brain. The subsequent identification of mono-amine-oxidase and its role in depression led to the introduction of MAO Inhibitors as a treatment. Similarly the discovery of the role gamma-aminobutyric acid in the brain led to the development

of benzodiazepines as anxiolytics and hypnotics in 1957. The identification of neurotransmitters led to the development of propranolol by James Black in 1962; other β -blockers for the control of blood pressure followed. About the same time the identification of histamine receptors led not only to the manufacture of antihistamines for the treatment of allergy but also to the discovery of cimetidine, also by James Black (1966), which by acting on histamine receptors in the stomach revolutionised the treatment of peptic ulcer.

FIND OUT MORE

Links to other sheets:

Theme C: Level 2 or level 3 sheets for drugs and drug groups are underlined.

Further Reading:

Weatherall, M, *In search of a cure, A history of pharmaceutical discovery*, (Oxford University Press, Oxford, 1990)

Mann, R D, *Modern drug use, An enquiry on Historical Principles*, (MTP Press Ltd., Lancaster, 1984)