**Pharmacy Practice: Lecture 1 Dr. Haider Raheem**

**Introduction: Historic Background**

**of Pharmacy Practice**

**Tracing the origins of pharmacy**

**Sumerians**

• The development of cuneiform writing on clay tablets during the third millennium BC included lists of drugs of animal, vegetable and mineral origin that were used in the management of diseases, and prescriptions with details of the ingredients used in their compounding.

• Many of the drugs listed were cited as having multiple uses since ailments were thought to be different manifestations of a condition.

• Use of medicines was carried out by priests (*ashipu*) and physicians (*asu*).

**Egyptians**

• The *Ebers Papyrus* (named after Georg Ebers, who purchased it in the nineteenth century) is a document dating back to 1550 BC, which describes prescriptions and modes of administration of drugs including gargles, inhalations, suppositories, ointments and lotions. Many of the drugs listed were included in the Sumerian documents.

• Use of medicines was carried out by priests. Imhotep who is regarded as the earliest physician, was the High Priest of Heliopolis.

**India**

• Ayurvedic medicine was first described around 800 BC. Documents list the use of drugs together with charms for expelling demons and make reference to the god of medicine, Dhanvantari.

• The *Charaka Samhita* includes reference to drugs of animal, plant and mineral origin used until the first century AD.

**China**

• In China, a comprehensive theory for diagnosis and treatment was developed.

• Manuscripts on silk and bamboo describe use of drugs of animal and plant origin.

• The text *Huangdi Neijing* listed the basic principles of pharmaceutical drug use in the third century BC.

• Shengnon Bencao Jing outlined basic theory of Chinese pharmacy.

• The Pen Ts’ao Kang Mu compilation presents details of drugs used in Chinese medicine in the late sixteenth century AD.

**Greeks and Romans**

• Just as the Egyptians revered Imhotep as the god–physician, the Greeks worshipped Asklepios as their god of healing.

• Later on, the use of medicines was carried out by the *rhizotomoi* (experts in medicinal plants), such as Empedocles, and the *pharmakopoloi* (preparers and sellers of drugs).

**Hippocrates**

• Considered to be the father of medicine.

• He is associated with a number of documents known collectively as the *Hippocratic Corpus* dating to 420–370 BC, which list 200–400 drugs of vegetable origin and describe the method of preparation of gargles, ointment and pessaries.

• His works placed emphasis on treating the patient with minimal reference to magical and religious powers.

**Galen**

• A physician around AD 160.

• He compiled medical knowledge of the time drawing on the documents by Hippocrates and Dioscorides.

• He described the use of formulations made up of numerous plants which were referred to as ‘galenicals’*.*

**The Arabs**

• In the Arab world, a large number of texts including documents related to medicine and works by Galen were translated into Arabic and that is how these documents have been transferred along history. Documents that were prepared included formularies, herbals and books on materia medica and toxicology.

• The use of medications consisting of complex formulations (galenic medicine) was continued.

• This required skilled preparation which was entrusted to apothecaries who opened their shops in the ninth century in Baghdad. The practice of the apothecaries was inspected by the state.

• Avicenna, a Persian philosopher, compiled the book *Canon of Medicine*, in which he merged the Greek and Arab works. The book describes the use of around 760 drugs.

• Albucasis, from the Arabic dominion in Spain, prepared documents which included a detailed description of the pharmaceutical process for the preparation of drugs in various dosage forms.

**Early definition of the pharmacy profession**

* After the establishment of apothecaries in Baghdad, the pharmacy profession started developing in Europe.
* Early Middle Ages: monastic medicine.
* Late Middle Ages: in the eleventh century, public pharmacies in southern Italy and southern France were established.
* Drug formulary produced by Nicolas of Salerno which described compound formulae of galenicals.
* 1231–1240: The Liber Augustalis, an edict on the profession of pharmacy, was issued by the German emperor Frederick II. The edict defined the separation of the pharmaceutical profession from the medical profession, described the official supervision of pharmaceutical practice and outlined an obligation by oath to prepare drugs reliably according to skilled art, and of a uniform, suitable quality.
* Early nineteenth century: retail pharmacies developed a separate manufacturing area, which included an area for extraction and purification, necessary for extraction of plant alkaloids such as quinine from cinchona bark used for malaria. Boehringer and Merck have their origins in community pharmacies in Stuttgart (1817) and Darmstadt (1827), Germany, respectively.
* Late nineteenth century: separation of the manufacturing business from the retail community pharmacy.

**Development of medicines**

* Seventeenth century: cinchona bark extract used for fever, chills – the principal active ingredient being quinine.
* Eighteenth century: foxglove plant used for the treatment of heart failure – digitalis.

**Analgesics and anaesthetics**

1804 Serturner isolated morphine from opium

1832 Isolation of codeine

1842 Ether used as an anaesthetic and later chloroform

1876 Stricker showed that salicylic acid had analgesic effects

1899 Development of aspirin by Bayer

1961 Development of ibuprofen

1969 Ibuprofen marketed by Boots

1983 Ibuprofen registered as an over-the-counter drug in the United Kingdom.

**Antibacterial drugs**

1891 Ehrlich coined the term ‘chemotherapy’; methylene blue used for malaria

1929 Antibiotic activity of penicillin described

1935 Sulphonamides developed by Domagk

1939–41 Florey and Chain synthesised penicillin

1944–5 Streptomycin and chlortetracycline isolated

1952 Isoniazid which was followed by other antituberculous drugs

1953 Phenoxymethylpenicillin

1956 Cephalosporin structure identified

1964 Cephaloridine marketed.

**Endocrine system**

1914 Crystals of thyroxine

1921–26 Isolation and crystallisation of insulin

1929 Isolation of oestrone

1934 Progesterone synthesised

1930–40 Isolation of different hormones from adrenal cortex

1959 First oral contraceptive

2006 Inhaled insulin marketed

2007 Pfizer announces that it will no longer market inhaled insulin due to marketing issues.

**Anticancer agents and immunosuppressants**

1946 Anticancer effect of nitrogen mustards described

1951 Mercaptopurine, an anticancer agent with an antimetabolite effect

1961 Azathioprine, an immunosuppressant

1970 Identification of paclitaxel

1992 Marketing authorisation for paclitaxel is granted

1990 Imatinib and trastuzumab developed

2000 Trastuzumab reaches registration

2002 Imatinib reaches registration

2006 Human papillomavirus vaccine hailed as the most important cervical cancer development since cervical screening.

**Therapeutic proteins produced by recombinant technology**

1982 Human insulin

1986 Human interferon alpha used in hepatitis B and C

1987 Human tissue plasminogen activator used in heart attacks, human growth hormone

1989 Erythropoietin used in anaemia

1991 Granulocyte–macrophage colony–stimulating factor used in neutropenia

1992–97 Human factors VIII and IX used in haemophilia

1994 Abciximab used for prevention of blood clot

1997 Rituximab approved for non-Hodgkin’s lymphoma

1998 Infliximab approved for Crohn’s disease and arthritis.

**Adverse effects**

1879–90 Sudden deaths during chloroform anaesthesia

1922 Jaundice associated with salvarsan

1937 People die after taking elixir of sulphanilamide which contained the solvent diethylene glycol

1955 Children in the USA infected with a polio vaccine due to a failure in the inactivation process

1961 Thalidomide – congenital malformations

1966 Chloramphenicol associated with blood dyscrasias

1997–99 Withdrawal of terfenadine and astemizole, the first antihistamines with a lower frequency of sedation that were marketed in the mid-1980s, due to increased risk of cardiotoxicity when taken with other drug therapy

2000 Withdrawal of cisapride which was a unique product with parasympathomimetic acivity that had a stimulating effect on serotonin receptors as well and was used in gastric conditions, due to increased toxicity in concomitant drug administration

2004 Withdrawal of rofecoxib, a COX-2 inhibitor, due to increased cardiovascular events

2006 Withdrawal of ximelagatran, the first oral anticoagulant drug to be released since warfarin, due to liver toxicity

2006 Development by Pfizer of torcetrapib, which had the main intervention of increasing high-density lipoprotein, stopped due to increased mortality

2007 Telithromycin associated with exacerbation of myasthenia gravis, occurrence of hepatoxicity, visual disturbances and loss of consciousness; revision in guidelines for its use.

**Development of pharmaceutical regulation**

**United Kingdom**

* 1963 As a result of the thalidomide tragedy, the Committee on Safety of Drugs was established
* 1968 Under the terms of the Medicines Act, the committee was renamed as Committee on Safety of Medicines (CSM). The Act stated that medicines required a licence to reach the UK market
* 1989 Medicines Control Agency (MCA) created
* 1994 Medical Devices Agency created
* 2003 Medicines and Healthcare Products Regulatory Agency (MHRA) established, bringing together MCA and Medical Devices Agency
* 2005 CSM became the Commission on Human Medicines (CHM), which provides advice to the MHRA.

**European Union**

* 1965 European directive for authorisation of medicinal products for human use presented
* 1975 Scientific Committee for Proprietary Medicinal Products for human use (CPMP) established
* 1993 Council regulation for the setting up of a European system for marketing authorisation of medicinal products and for the establishment of a European agency
* 1995 The European Medicines Agency (EMA) opens in London, UK.

**United States of America**

* 1906 US Pure Food and Drugs Act which required information on contents and purity of medicines
* 1927 Food, Drug and Insecticide Administration takes up regulatory functions
* 1930 Food, Drug and Insecticide Administration renamed the Food and Drug Administration (FDA)
* 1938 As a result of the sulphanilamide elixir tragedy, the Food Drug and Cosmetics Act was passed which required approval by the FDA before a new drug product was marketed
* 1988 Food and Drug Administration Act which established the structure and responsibilities of the agency.

**International**

* 1989 At the WHO Conference of Drug Regulatory Authorities (ICDRA) plans for discussions between Europe, Japan and the USA on harmonisation started
* 1990 The International Conference on Harmonisation (ICH) was established. It is a forum of constructive dialogue among the three regions which aims at facilitating exchange, dissemination and communication of information.