Chapter 1

Introduction to Pharmacology: Drug Regulation and Approval

History of Pharmacology

- Records exist in every culture dating to antiquity
- Records describe use of plants (herbs) to relieve symptoms.
- Dark Ages show few records; still using herbs

Pharmacologia sen Manuducto and Materiam Medicum

- Written by Samuel Dale in 1693
- First recorded reference to pharmacology

Modern Pharmacology Began in Early 1800s

- Chemists isolated pharmacological substances from natural substances
- Effects on animals studied
- Early researchers used themselves as test subjects

Pharmacology Recognized as Distinct Discipline

- First department of pharmacology established at Estonia in 1847

John Jacob Abe

- Father of American pharmacology
- Founded first pharmacology department in United States at University of Michigan in 1890
Twentieth Century to Present

- Drugs synthesized in laboratory
- Drugs tested for relatively short time
- Understanding increased of how drugs produce their effects
- Focus is on improvements in quality of life

Pharmacology

- Study of drugs
- How drugs are administered
- Where drugs travel in the body
- Responses drugs produce

Interrelated Subject Areas

- Anatomy and physiology
- Chemistry
- Microbiology
- Pathophysiology

Pharmacology Is Challenging and Always Changing

- 10,000 drugs currently available
- Each drug has its own characteristics
  - Therapeutic applications
  - Interactions
  - Side effects
  - Mechanisms of action

Pharmacology Is Challenging and Always Changing

- Many drugs prescribed for more than one disease
- Drugs elicit different responses depending on individual factors
  - Age
  - Sex
  - Body mass
  - Health status
  - Genetics

Therapeutics and Pharmacology Are Closely Connected

- Therapeutics is concerned with
  - Prevention of disease
  - Treatment of suffering
- Pharmacotherapy is the application of drugs for
  - Disease prevention
  - Treatment of suffering
Traditional Drugs Are Chemical Agents
- Synthesized in a laboratory
- Produce biological responses in the body
  - If desirable response—therapeutic
  - If undesirable response—adverse

Examples of Biologics
- Hormones
- Monoclonal antibodies
- Natural blood products and components
- Interferon
- Vaccines

Complementary and Alternative Therapies
- Natural plant extracts, herbs, vitamins, minerals, dietary supplements
- Acupuncture, hypnosis, biofeedback, massage

Advantages and Disadvantages of Prescription Drugs
- Advantages
  - Health-care provider examines the client and orders proper drug.
  - Amount and frequency of drug is controlled
  - Instructions on use and side effects of drug are discussed
- Disadvantages
  - Require a prescription to obtain
  - Need for health-care-provider appointment

Advantages and Disadvantages of OTC Drugs
- Advantages
  - No health-care provider appointment required
  - Often less expensive than prescription drugs
- Disadvantages
  - Client may choose wrong drug
  - Client may not know reactions or interactions
  - Ineffective treatment may result in progression of disease

Prior to 19th Century
- Few standards or guidelines to protect the public
  - Some drugs contained hazardous levels of
    - Dangerous substances
    - Addictive substances
**History of Pharmacology**

**United States Pharmacopoeia (USP), 1820**
- First comprehensive publication of drug standards
- Summarized standards of drug
  - Purity
  - Strength
  - Directions for synthesis

**National Formulary (NF), 1852**
- Established by American Pharmaceutical Association (APhA)
- Focus was on pharmaceutical ingredients

**USP and NF Merged in 1975**
- Formed United States Pharmacopoeia–National Formulary (USP-NF)
- Official monographs and interim announcements published regularly
- Full bound version printed every five years

**United States Develops and Enforces Tougher Drug Laws, 1900s**
- Biologics Control Act, 1902
  - Standardized serum and blood-related products
- Pure Food and Drug Act, 1906
  - Government controls labeling of medicines
- Sherley Amendment, 1912
  - Prohibited drugs labeled with false therapeutic claims

**United States Develops and Enforces Tougher Drug Laws, 1900s**
- Food, Drug, and Cosmetic Act (1938) and amendments
  - Thorough testing of drug
  - Proof of safety and efficacy of drug
- Dietary Supplement Health and Education Act, 1994
  - Controls misleading industry claims

**Food and Drug Administration (FDA)**
- Officially established in 1988
- Agency of US Department of Health and Human Services in 1988
### Center for Drug Evaluation and Research
- Branch of FDA
- Determines safety and efficacy of drugs
- Pharmaceutical laboratories must solicit approval from FDA before marketing a drug

### Center for Biologics Evaluation and Research (CBER)
- Branch of FDA
- Regulates use of biologics (serums, vaccines, and blood products)
- 1986 Childhood Vaccine Act result of CBER work

### Center for Food Safety and Applied Nutrition (CFSAN)
- Branch of FDA
- Oversees herbal and dietary products
- Enforces 1994 Dietary and Supplemental Health and Education Act
  - Regulation not as close as Food, Drug, and Cosmetic Act

### Four Stages of Approval for Therapeutic and Biologic Drugs
- Preclinical investigation
- Clinical investigation
- Review of new drug application (NDA)
- Postmarketing surveillance
- Amount of time for approval varies

### Preclinical Investigation
- Involves laboratory research
- Tests done on cells and animals
- Determines drug-dose range
- Examines adverse effects
- Results are considered inconclusive

### Clinical Investigation
- Longest part of approval process
- Termed “clinical-trials phase”
- Evaluates human benefits
Review of New Drug Application (NDA)

- Average review time 17–24 months
- Drug approved: process continues
- Drug rejected: process suspended

Post Marketing Surveillance

- New drug placed on market
- Surveyed for harmful effects in larger population
- FDA holds annual public meetings

Reasons for Delays in FDA Drug-Approval Process

- Outdated guidelines
- Poor communications
- Insufficient staff to handle workload

Prescription Drug User Fee Act, 1992

- Established on five-year trial basis
- Drug and biologic manufacturers provide drug-user fee
- FDA hired more employees
- FDA restructured its organization

Results Successful

- Double the number of drugs approved
- Some review times cut by half

FDA Modernization Act, 1997

- Reauthorized Prescription Drug User Fee Act
**Drug Approval Process in Canada: Six Steps**

- Preclinical studies
  - Living tissue
  - Small animals
  - Then humans

**Drug Approval Process in Canada: Six Steps (continued)**

- Complete drug submission to Health Canada
  - Safety and effectiveness information
  - Therapeutic benefits
  - Adverse reactions
- Committee of experts reviews drug submission
  - Benefits
  - Drug risks

**Drug Approval Process in Canada: Six Steps (continued)**

- Health Canada reviews information about drug product
  - Passes important details to health practitioners and consumers
- Health Canada issues permits to market drug product
  - Issues notice of compliance (NOC)
  - Issues drug identification number (DIN)

**Drug Approval Process in Canada: Six Steps (continued)**

- Health Canada monitors drug postmarketing
  - Effectiveness
  - Concerns

**Similarities Between Drug-Approval Processes in United States and in Canada**

- Preclinical testing of drug
- Proving safety and effectiveness of drug
- Monitoring drug after placement on the market