Introduction:

Introduction to central nervous system Bertra G K. et al.

The human brain is an assembly of interrelated neural systems that regulate their own and each others activity in dynamic and complex fashion. Major parts of CNS are cerebrum, limbic system including basal ganglia, thalamus, hypothalamus, midbrain and reticular formation, cerebellum, pons, medulla oblongata and spinal cord.

The CNS is not only concerned with the regulation of specialized functions like circulation, digestion and respiration but it also modifies the psychic reactions such as feeling, attitude, thoughts and memory. The ability to think logically, to learn from past experience and to communicate appropriately is the unique qualities of man and can be attributed to the development of the highly specialized central nervous system.

Drugs acting on CNS are important from clinical point of view. The action of drug on CNS is particularly challenging because it demands an understanding of cellular and molecular biology of the brain. Although the knowledge of anatomy, physiology and chemistry of nervous system is far from complete, the acceleration of interdisciplinary research on CNS has led to remarkable progress.

Drug acting on central nervous system were among the first discovered by primitive humans and are still in most widely used therapy, many drugs acting on the CNS are used without prescription to increase one’s sense of well-being.

The mechanisms by which various drugs act in the CNS have not always been clearly understood. Since the causes of many of the conditions for which these drugs are used (Schizophrenia, anxiety, depression etc) are themselves poorly understood, it is not surprising that in the past much of CNS pharmacology has been purely descriptive. In the last three decades, however, dramatic advances have been made in the methodology of CNS pharmacology. It is now possible to study the action of a drug on individual cells and even single ion channels within synapses. The information obtained from such studies is the basis for several major developments in studies of the CNS.
Drug therapy affecting CNS  

Rang HP et al.

Following classes of the drugs are acting on the central nervous system.

1. CNS Depressant
   (A) General and local anesthetics
      1. Inhalation anesthetics
      2. Intravenous anesthetics
      3. Local anesthetics
   (B) Sedatives and Hypnotics
      1. Alcohol
      2. Barbiturates
      3. Non-Barbiturates
   (C) Anti-epileptics

2. Drugs used in psychiatric disorders
   (A) Major tranquillizers
   (B) Minor tranquillizers
   (C) Anti-depressants
   (D) Psychotomimetics
   (E) Psycho stimulants

3. Drugs used to relieve pain
   (A) Narcotic Analgesics
   (B) Non-Narcotic Analgesics

4. Drugs used for Parkinsonism and other motor disorders

1.1 PSYCHOSIS

Psychosis is a mental disorder which involves striking disturbances of thought, perception, affect, and behaviour. The expression of psychotic symptoms varies over time and across patients, however the cumulative effects of the illness are always severe and usually long lasting. There are various types of psychotic disorders such as anxiety, bipolar disorder (manic disorder), depression and schizophrenia. These disorder a briefly discussed in the following sections.
INTRODUCTION

ANXIETY
Anxiety is a normal response to psychological stress induced by either physical or perceived threat. However, a malfunctioning anxiety response could lead to anxiety disorders. Anxiety disorders are further divided into five types; such as panic disorder, social phobia, obsessive compulsive disorder, generalized anxiety disorder and posttraumatic stress disorder. Patients suffering from anxiety disorder are usually treated either by medication or psychotherapy.

MANIA OR BIPOLAR DISORDER
Mania or bipolar disorder is a brain disorder that causes unusual shifts in a person’s mood, energy and ability to function. During a manic episode, the mood disturbances are severe enough to cause significant impairment in occupational functioning or in otherwise normal social activities. Bipolar disorder is further classified into two groups namely Bipolar I and Bipolar II. Bipolar I is characterized by one or more manic or mixed episodes. Bipolar II is characterized by recurrent episodes of major depression and hypomania. Bipolar disorder affects approximately three to five percent of the world’s population, and affects both sexes equally in all age group.

DEPRESSION
Depression is defined as a feeling of intense sadness. Depressed individuals tend to be obsessed with personal failings, are apathetic and socially withdrawn. Depression disorder can be transmitted in the form of negative emotions from living or non-living beings to susceptible host. Therefore, depression is also known as communicable disorder. Symptoms of depression disorder can last periods of time, sometimes several two years.

Antidepressants may be classified in to four groups.

1) Reversible MAO - A inhibitors
   Moclobemide, Clorgyline

2) Tricyclic antidepressants
   A) NA and 5 – HT reuptake inhibitors
      Imipramine, Amitriptyline, Trimipramine, Doxepin, Dothiepin,
      Clomipramine
   B) Predominant NA reuptake inhibitors
      Desipramine, Nortriptyline, Amoxapine
3) Selective serotonin reuptake inhibitors (SSRIs)

Fluoxetine, Fluvoxamine, Paroxetine, Sertraline, Citalopram

4) Atypical antidepressants

Trazadone, Mianserin, Mirtazapine, Venlafaxine, Tianeptine, Amineptine, Buprop

SCHIZOPHRENIA

Schizophrenia is a complex cognitive disorder comprising of a variety of alterations in attention, working memory, language, response monitoring and inhibition. Schizophrenia is treated as a debilitating disorder of the central nervous system. Its symptoms are divided into two classes namely positive symptoms and negative symptoms. Positive symptoms include hallucinations, delusions, conceptual disorganization, where negative symptoms include social withdrawal, blunted affect, and poverty of speech. This disorder reduces the ability of the individual to interact with the social. Schizophrenia affects about 1% of the world's population. All these types of mental disorders mentioned above are treated with antipsychotic drug that will be described in the following section.

All these types of mental disorders mentioned above are treated with antipsychotic drug that will be described in the following section.

1.2 ANTIPSYCHOTIC DRUG

The term antipsychotic is applied to a group of drugs used to treat psychosis. These classes of drugs were originally called 'neuroleptics' (from the Latin root which mean to grasp the neuron). Antipsychotic drugs are generally divided in two types; that is typical antipsychotic drug and atypical antipsychotic drug.

TYPICAL ANTIPSYCHOTIC DRUG

Typical antipsychotics are also known as major tranquilizers because of their tranquilizing and sedating effects when taken in large doses. Typical antipsychotic drugs are effective primarily against positive symptoms of schizophrenia. Such drugs include haloperidol (HP), chlorpromazine, perphenazine; thioridazine and trifluoperazine are examples of typical antipsychotic drug. Chlorpromazine was the first typical antipsychotic drug used in 1952 to treat
schizophrenic patients. Antipsychotic properties of typical antipsychotics are achieved through the antagonistic effect on dopamine receptors. The typical antipsychotic drugs used to treat schizophrenia are highly effective. In particular, HP, the most widely used typical antipsychotic is very efficient in treating the positive symptoms of schizophrenia. The most predominant among these symptoms are dystonia, parkinsonian-like syndrome, and tardive dyskinesia.

ATYPICAL ANTIPSYCHOTIC DRUG

Atypical antipsychotic drugs are used to treat schizophrenic patients and results less extrapyramidal side effects. Compared to the older ‘typical’ antipsychotic, the atypical antipsychotic drugs are equally effective against the positive symptoms and the negative symptoms of schizophrenia. Atypical antipsychotic drugs block both dopamine and serotonin (5-hydroxytryptamine) receptors. These combined effects on both dopamine and serotonin (5-hydroxytryptamine) receptors explain the lower extrapyramidal side effects of atypical antipsychotic drugs. Examples of atypical antipsychotic drugs are ariprazole, risperidone, clozapine, olanzapine, quetiapine and ziprasidone.

MARTA (multi acting receptor targeted agents)
- clozapine, olanzapine, quetiapine

SDA (serotonin-dopamine antagonists)
- risperidone, ziprasidone, sertindole

Selective D2/D3 antagonists
- sulpiride, amisulpiride

DEVELOPMENT OF NEW ANALYTICAL METHODS:

A regulatory analytical procedure is the analytical procedure used to evaluate a defined characteristic of the drug substance or drug product. An alternative analytical procedure is an analytical procedure proposed by the applicant for use instead of the regulatory analytical procedure.

Analytical chemistry based on TWO aspects:

➢ Qualitative analysis: To establish the presence of a given element or functional group in a sample (Inorganic / Organic).
**INTRODUCTION**

- **Quantitative analysis**: To establish the amount of the given element or compound in given sample.

**Methods Of Detecting Analysts**
- Physical means
- Mass
- Color
- Refractive Index
- Thermal Conductivity

- With Electromagnetic Radiation (spectroscopy)
  - Absorption
  - Emission
  - Scattering

- By an electric charge
  - Electrochemistry
  - Mass spectrometry

**VALIDATION OF ANALYTICAL METHOD:**
As defined by the USP, method validation provides an assurance of reliability during normal use, and is sometime referred to as “the process of providing documented evidence that the method does what it is intended to do.” The objective of validation of an analytical method is to demonstrate that the procedure, when correctly applied, produces results that are fit for purpose. To be fit for the intended purpose, the method must meet certain validation characteristics. Typical validation characteristics, which should be considered, are: selectivity (specificity), linearity, range, accuracy, precision, limit of detection, limit of quantization, ruggedness, robustness and system suitability testing.

Validation is required in following situations:
- When totally new process;
- New equipment;
- Process and equipment which have been altered to suit changing properties;
- Process where the end product test is poor and an unreliable indicator of product quality.