UNIT-Ist PHARMACEUTICS

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HISTORICAL BACKGROUND AND DEVELOPMENT of PROFESSION of PHARMACY

Pharmacy → The science or practice of the preparation and dispensing of medicinal drug.

→ Pharmacy comes from a greek word pharmacan means 'drug'.

→ Dispensing → distribute or provide to a no. of people

Pharmaceutics →

→ It is discipline of pharmacy that deals with the process of turning a NCE (New chemical entity) old drugs into a medicine safety and effectively by patients.

→ It is also called as "Science of dosage form design".

History of Pharmacy

Ancient Era	Empiric Era	Industrilization Era	Patent Era	Biotechnology + Genetic eng era
the begenning time to 1600 AD	1600 - 1940	1940 - 1970	1970 present	New horizen

1) Ancient Era :- Used leaves, mud, cool water to stop bleeding. they used to method to animal how they heal their wound. the pharmacy begins from.

→ In babylover earlist record of practice of pharmacy by priest, pharmacist was kept.

→ Hippocrates → father of medicine.

→ Mithredatis → father of toxicology [Mathieu orfila].

→ Cosmos & Damian → Saints of pharmacy and medicine.

After fall of Roman empire

division of pharmacy and medicine evolved.

→ Ebers papyrees written formulas for more than 800 remedies.

Major advances in Pharmacy [During their period] :-

1. formulary
Continuation of documentation of knowledge of specific drugs information used by pharmacist.

2. Dosage form
Well no longer harvested from herb gardens. eg. Syrup.

3. Pharmacy shop.
1st appeared in Baghdad in 754 AD.

In ancient India some of drugs were of vegetables animals and minerals origin. They were prepared empisically by few experiments person knowledge of that medical system was usually kept secret with in a family. There were no scientific methods of standardization of drugs

→ At the end of this era pharmacy was separated from medicine.

2. Empiric Era :-

→ The pharmacopoeia was a regulatory tool for pharmacist Benzamin franklin stated first hospital with pharmacy and 1st pharmacist was Jathan Roberts

→ Chemical were identified like N_2, Cl_2 Mosphine pencellin.

The western or so called Allophatic system

comes into India with british trades who later become rules. Under british rule this system got state patronage.

Before 1940, Initially all drugs were impacted from Europe. Later some drugs began to manufactured in this country.

1901	1903	1907
Est of Bengal chemical and Pharmaceutical work at Calcutta by Achanya P.C Roy	Small factory at Parel (Bombay) by prof. T.K. Gujjar	Alembic chemical works at Baroda by prof. T.K. Gujjar

→ Drugs were mostly exported in crude from and imported in finished form. During world war-I (1914-1920) import of drugs were cut off. In case of absence of any respichon on quality of drugs imported, manufacture took advantage of the situation and consequence.

1) Infeior quality medicines and adulterated drugs were dumped.
2) Markets were full of useless drugs were sold by unqualified mens.
3) (a) Poisoning due to quiminet
   (b) Silling of chalk powder tablets in place of quimine.

few lens were in these having indirect bearing on drugs but were insufficient 1878 opium deals with cultivation of poppy and the manufacture, transpoit (export sale of opium.

1894 Indian Transf act → Levy of customers duty on goods including drug medicines imposted or exported.

1919 Poisons Act → regulated the impact possession and sale of poison.

3. Industrilization Era :-

a) Civil war b) World war I [1940-1970].

→ More people got enjured ill. More production of medicine were made through industrials machines.

→ Scientific research, investigation on medicines and their effect was dones.

→ On the basic of this research many new drug and old drugs were being used which caused more reactions.

→ The development of manufacturing of pharmacy begin.

→ Spandardization, biologically prepared products complete chemical syuthesis and increase use of parental modification.

4. Patient Care Era :-

→ Beginning concentrated on research of to develop new medicines research or medication was done.

→ News drugs were develop.

→ Head alot of adverse seaction to drugs. So drug review and monitoring was done.

→ Plist had great role in dispensing medicine and patient education.

5. future of Pharmacy.
→ Research in area of biotech and gene therapy is conducted medicine are being produced through recombinate DNA technology
→ New therapies for cancer, anaemia, hepatitis are being introduced.

6. History of Pharmacy education in India :-
→ The earliest traditional system of medicine practiced in India have been Ayurveda and Siddha the cause from west Asia colonical period.

Drug Enquiry Committee :-
Gov. of India formed a comitee on 11th August 1930 named drug enquiry comitee under the chairmanship of late Lt. R.N Chopra to deal with many problems of Pharmacy. The 1st report of commitee was published in 1931 saying that there was no recognized profession of pharmacy. The pharmacy practice was done by the person called compander. By the effect of this report prof. M.L. schroff enitiated to start a pharmacy education at the university level in Banaras Hindu University (1932).
→ After pharmacy education started in the country graduate development of administrative profession level and industrial level have been done in order to promote Pharmacy profession in India.

1935 → United province pharmaceutical associations was established to discuss related matter at National level.
1937 - Andhra University.

1938 - Modral University.
1939- Scientific journal stated by M.L. Shroff named Indian Journal of pharmacy
1940- All India Pharmaceutical Congress Association was established with the intention to Publish pharmacy as a whole by conducting conference at different places.
→ Gov. of India braght 'Drug' to regulate import sale of drugs the finale adopted as drug and cosamis Act 1943- Bombay, 1944- Bhmive,

1945- was braght to standardize pharmacy education in India.
1946- Pharmacopecial list was published under chairmanship of R.N. chopra
1948- Pharmacy act was published to green the pharmacy education in India.
it

D.Pharma	B.Pharma
2yrs	3 yrs

1948- Indian Pharmacopoeia committee was constitiled in 1949- Pharmacy cancil of India was established under pharmacy act 1948 to regulate the standard.
In 1954- Education Regulation come into force in some state for regulation the stand of Diploma Pharmacy At present 1600 institution offering varios pharmacy progsammis like B.Pharma, D.Pharma, M.Pharma the syllabus of Pharmacy education is focussed on neds and demands of todays pharmaceutical act a pharma version 2010 released

by APJ Kalam in 2003 (Mumbai) have proposed new activities to shape the future of pharmacy profession new practice of PG programmes in hospitals pharmacy are also done. Pharma 5 yr of training and 1 year internship. Beside this doctorist field like pharmaceutical chemistry pharmaceutics, pharacognosy etc.

History of Pharmacy in Abroad.

Earliest known compilation of medicinal substance was the 'sushruta samhita'.

→ Ancient egyption pharmacological knowledge was recorded in various papyri such as ebers papyri of 1550 BC.

→ In ancient greece diodes was one of several men studying medicinal properties of plants.
Greek physician discoside is famous for writing a 5 volume book.
Latin translation 'De materia medica' was used on basic of medival text.

→ Earliest chinese Three manual nature medico is Shennong Benco jing (1st century AD) prescription earlier literature include list of specific ailments contained recepies of 52 ailerent (168 BC). further details of chinese pharmacy may be fand in pharmacy in china article.

→ Japan → At the end of Ashoka Period (538-710) and early Nara period (710-794) the men who fulfilled roled similar to those of modern pharmacist were highly respected.

→ The place of pharmacist in society was expresly defined in Taiho code (701) and restated in

in yoko code (718).

The P'eist and even P'eist assistant were assigned status supuor to dll the other in health related fields — the pharmacist was ranked above the 2 personal physician of the emperor.

In Baghdad (Iraq) → 1st pharmacist or drug-shop were established in 754.

In Europe pharmacy like shops began to appear during 12th century. 1st Pharmacy in Europe was opened in 1241. in Germany. The oldest claimed to have been set up in 1221 in church of Santa Masia Novella in Florence. Italy which now hosts a perfume museum.

WHO has contributed effectively towards encouraging and defending the role of pharmacist world wide. WHO has recommended a special role of P'ciest particularly in quality assuance of and safe adulteration of drugs.

In Malysia → which is one of the leading countries has acute shortage of pharmacist

2006 ratio = $\frac{\text{P'cist}}{\text{population}} = \frac{1}{6207}$

Doctor themselves dispence resdications as part their professional practice.

In African Countries (Ghana) Shortage of P'ciest is even worse - 619 p'ciest are serving 2.9 million peoples.

In 1948 Univ. of Pb. was institution to develop pharmacy departonent in Pakistan after independence. The 1st degree was of 3year pharmacy bachlor course programe which was later extended 4year in 1978, 1979. 9 same colleges. Karachi Uni. and peshwar University.

Pharmacy as a Career

It is the branch of science which deals with the comparding and dispencing of the drugs. In Greek pharmakon mean drug. Now a days their is a great scope in the field of Pharmacy.

Scope in the field of Pharmacy:-

1) Pharmaceutics company as enterpreneur →
→ A person who has done his/her degree in the field of pharmakon open his/her pharmaceutical company.

2) Academics → Person who has done his/her studies in the field of pharmacy can work as a lecture, ass. professor, open his/her pharmaceutical company.

3) Can start an institute → Person who has passed his/her Carrier in pharmacy can open education institute to serve the students.

4) Regulatory Dept. → Person who has passed his/her Carrier in pharmacy can try his luck in the regulatory dep. i.e government Seeter.

There are no. of jobs in the government sector for the pharmacy aspirants like drug Inspector, drug control, labs, etc.

5. Pharmaceutical Industries → Pharmaceutical industries provide the maximum no. of scope to the people who have done their studies in the field of pharmacy. The types of jobs in the pharmaceutical industries are as follow:-

- Research and development
- Production
- Analysis
- Marketing
- Pharmacovigilance

- Research and Development →
It is the branch in the pharmaceutics industries which is responsible for the research and development factor of the drug people in this branch of pharmaceutical industries have need to research using articles, newspaper etc or either resources to get material / thought to development new drugs.

- Production →
It is the branch in the pharmaceutics industries which is responsible for the production of drugs. People in this branch of pharmaceutical industrial have need to produce the maximum result using the existing facilities or machinary.

- **Analysis**
  It is the branch in the pharmaceutical industries which is responsible for the analysis of drug produced by production. People in this field (QA) or (QC) works during production period and after production periods to keep the check on the drug produced.

- **Marketing**
  It is the branch of the pharmaceutical industries which is responsible for the marketing of the drugs produce to the retailer a hospitals. People from this branch has need to make food relation a customers to make good business or industries profeet.

- **Pharmacovigelance**
  It is the branch of pharmaceutical industries which is responsible for the collection, detection monitoring and prevention of adverse effects by pharmaceutical products. It is the common branch in the pharmaceutical industries.

6) **Pharmacist**
After doing studies in the field of pharmacy a person become a pharmacist, who can practice pharmacy to produce useful drugs/ medicine.

Introduction to Pharmacopoeia

Pharmacopoeia comes from greek word 'Pharmakon' means drug and poiea means to make. Therefore it can be defined as any recipe or formula and standard required for preparation of drug.

The term Pharmacopoeia was 1st used in 1580 in a book or drug standard poicully in Italy. The books containing the standard of drugs and other related substance are known as pharmacopeia and formulaties collectivity, these book are known as "Drug compendes".

It contain the list of drugs and other related substances regarding their source, discription, tests, formula for preparation book are prepared under the authority of gov. of respective countries.

These books are modified time to time to introduce the information available. In order to introduce new product and to keep the size of book with in limits it becomes nessacery to admit certainety ave used drugs and act in each new addition of these books certain new monogeaph are added while elder are removed. for its preparation the expert opinion of medical practitioner, teacher, pharmaceutical manufacturing in obtained.

The drug compendia can be classified as

Official

→ official are the compilation of drugs and other related substance which are recognised as legal standard of purity quality and strength
eg. IP, B.P., USP, USSR

Non-official

→ Book other than official drug compendia which are used as second drug reference source of drug
eg. Marek Index, Remingtons P'ceuticals Science

1) National formulary of India

Committe was constituted in Nov 1956 who was assigned the work to complete the formulary. The openians of medical associations hospitals, teaching institutions and manufactures were invites and finalised by committee. It was printed in India by manegs. gov of India press, shimla in 1960.

2) Pharmacopoeia of India

- In 1946 Gov. of India Published P'copoeia list (as a supplement of BP)
- After this list gov. of India. 1st I.P. published in 1955.

3) Merck Index

It is encyclopedia of chemical drugs biolicals. The 1st edition in Published in 1889 and IInd edition is published in 1989 by merck and Index Rolway. N.S us it.

→ P'copoeials of Varias countries —

- The Indian Pharmacopoeia.
- The British Pharmacopoeia.
- The United State Pharmacopoeia.
- The Extra Pharmacopoeia
- The Internation Pharmacopoeia
- The European Pharmacopoeia.

IP → The history of Indian P'copoeia began in 1883 when committee of fast India company dispensary recommended the published of P'copoeia and Bengal pharmacopoeia was published in 1844. which mainly listed most of commonly used in indigenars remedies.

1868 both drugs of BP and Indigenars used in India.
1869 suplement of above publication with verbualar name
1885 BP was made official in India.
1927 DFC recommended published P'copoeia. National P'copoeia.
1946 Govt. of India Published pharmacopoeia list
1948 constituted permanent IP
1955 1st edition of I.P.
1966 2nd edition of IP (Revised form)

The work of revision of it as a compilation of new addition was taken up simultaniasly under chairman of Dr. B.N. Ghath proff. P'copoeia RG kar (Medical college calcutting) died in 1958. After B.N. Ghosh, Dr. B. Mukherji was appointed as chairman UP committee its supliment published in 1975.

On 30th June 1978. IP committee was reconstitute by Gov of India, ministry of health and welfare under chairman of Mitya Nand, Director [central drug research institute)

The committee assigned work for help preperation of 3rd edition of P'copoeia.

3rd edition 1985 - followed by its addenclined in 1989 and 1991.

In vol Ist and vol IInd

(1) Volume I → contains legal notice preface, acknowlegement, introduction, general notices and monograph from A to P.

(2) Volume II → contains monograph from a to z appendices Content of appendis.

for the preparation of IP, the P'copoeia of other countries like BP, USP, USSR etc were consulted. The passon working in P'ceutical Industry, drug control lab research and teaching also actively participate.

I.P 1996 → 4th edition followed by its eddendum 2008.

↓

Suppliment for retains any products in good to 2005.

I.P- 2007 → 5th edition followed by addend 2008.

I.P. 2010 → 6th edition followed by addl 2001

DVD of IP - 2010

IP 2012 - with DVD and 7th edition.

The 7th edition of IP was published by IP commosion of behalf of GOI, ministry of Health welfare.

Under the drugs and cosmetics act 1940, IP is an official book which contain standard of drugs and related substances included in P'copoeia. It helps in licensing of manufacturing inspector of distribution of medicise.

→ IOP 2014 is presented in 4 volumes.

Keep feature

1st time IPC has introduce 19 Radio P'ceutical monograph. standard for new drugs are used under National Health Progsammus IP 2014 has 2667 monograph out of monograph out of which 577 consisting of API, excipients, dosage form, herbal products etc.

IP monograph of an official substances or preparation includes articles defination, discription, identification, packing, storage, chemical spactrue, molecular formula, along with IUPAC name of substance are also mentioned in case of API.

1st time IP 2014 included DVD-ROM.

577 → New monograph
134 → API
161 → formulation monograph
11 → Antiviral Monograph

10 → Antibiotic Monograph
19 → Anticancer Monograph
05 → Monograph on Biotech.
19 → New chapters and about 200 I.P. specimen.
19 → New Radio Pharmaceutical Monographs

A separate volume of vetering products is also introduce for easy access.

The following monograph incarporated are not present in other pharmacopoeia like drotaverin hydrochloride, Rifaxi done tablets.

It is assumed that this addendum would play a significant role in improving quality of medicine which is turn, improve quality of life of public and speed up development of pharmaceutical industry. The drug and other related substances prepared by pharmaceutical manufactured must comply these standard.

British Pharmacopoeia

It come into existence in 1864 and was published by general council of Medical education and registration of United kingdome.

The responsibility of publishing the B.P has rested upon the genral Medical cancil since medical act 1858. The provision and duties of this cancil are contained in Section 47 of Medical Act 1956. According to recommendation of committee.

Prescription

Prescription

Prescription is a written order practitioner from a registered medical practioner or other properly licensed such as dentist and veterinarian to a pharmacist to compound and dispence a specific medication for the patient. The order is accompanied by the direction for the pharmacist prepare a specific type and quantity of preparation for a patient. The prescription also include the direction for patient regarding mode of administration of the medicine is dispensed for him. Thus prescription is a media to which treatement is provided for a patient by the combined skilled and services both the physician and pharmacist.

The Priscription are genrally written in english language but latin words and abbreviation are also used in order to save him. So, it become necessary for a pharmacist to become familier with common latin words and abbreviation used by prescriber while writing the prescribe.

Different parts of prescription →

Priscription are genrally written on a typical format which are usually kept as pads a typical priscription consists of following parts.

i) Date
ii) Name, Age, Gender And address of the patient.
iii) Superscription
iv) Inscription
v) Signature
vi) Subscription
Renewal instruction
Signature, address and Registration no. of the prescribe.

1) Date → It helps a pharmacist to find out the date of prescribing and dat of presentation for filling the preseriphon. The priscriphon which prescribe Narcotic. On other habit forming drugs must be the ~~drug~~ date so as to avoid the misuse of prescriphon. It is prescut by the patient a no. of time for dispensing.

2) Name, Age, Gender, & Address of the patient →
It must be written in the prescriphon because it serves to identify the psph the same may be includes by the pharmacist after proper enquiry from the patient. Age and gender of the patient, specially in the case of children help the pharmacit to check the prescribe close of midicatin. In some cases, the weight of the patient also be required in order to calculate the appropriate close.

3) Superscription → It is represented by the symbol ℞ which is written before writing the prescriphon. ℞ is an abbreviation of latin word 'recepi' meaning 'you take'. In days the be originated from the ~~origin~~ sign of Jupiter (God of healing).
This symbol was complayed by the ancient in requesting God for the quick recovery of the patient.

4) Inscription → This is the main part of the presciphon order contain the name and quantity of the prescribed ingredients are generally written in english language but common abbreviation used can be written in english and latin language.

the name of each indegsient is written on a separate line along with its quantity. In compex prescription containing several endigsients. The inscription is divided into following parts.

i) Base → The active medicament which are intended to produce actiu therapeutic effect.

ii) Adjuvant → It is included weither the action of medicament or to improve the palatability of the preparation.

iii) Vehicle → It is included in prescription either to dissolve the solid indegsient or to increase the volume of preparation.

c) Subscription → This ~~comprise~~ compriese direction to the pharmacist for prepaing the prescription and no. of doses to be dispence. These days the prescriper are amitting the specific instruction to the pharmacist because the majority of the piscription are not compunding and dispense.

d) Signature → This is ~~concept~~ consists of the direction to be given to the patient regarding the administration of the drug. It is usually written as 'sig' on the piscription. ~~containing narcotik and other habit forming drugs to prevent its misuse~~ The instruction given in the prescription given are required to pansfer label of the container in which medicaments is to dispence so that patient can follow it. The instruction may include the following it's

i) The quantity to be taken.
ii) The mode of administration.
iii) The ~~mode~~ of frequency of administration.
iv) The special instruction such as dilution direction.

7) Renewal instruction → The prescribe indicate every prescription order rather it may be general and it so how many times. It is very important particularly in the prescription containing narkotic and other habit forming drugs to prevent its misuse.

8) Signature, address and Registration No. of the prescriber → The prescriber must bear the signature of the prescriber along with its registration number and address. It is very important particularly containing the narkotic and other habit forming drug to prevent its misuse.

- primo mane → early morning
- mane → morning
- Omni mane → every morning
- Omni nacte → every night
- Inter nacte → during night
- nocte → at night
- Omni hara → Up. prevent hars
- Omni quata hora → every four hars.

example of Prisciption

General Hospital

Date — 22-08-2018
Name — Mso Ram Sharma
Age — 39 years.
Sex — Male
Address — 457, sector-15, chandigash

℞ (supurscription)

Pottasium Bromide 8gm
Tincture Nux Vomica 8ml } (Inscription)
Chlaroform water 9.5 120 ml
fiat mixture (subscription)
sig. Cochleare magnum ter in die
past cibos sumendus (signature)

(signature of prescribed)
A.C Agrawal M.D
Regd. NO — 102341

Handling of prescription

The following procedure should be adopted by the pharmacist while handling the prescription for compounding and dispensing

i) Receiving
ii) Reloading & checking
iii) Collecting & weighing the material.
iv) Compounding, labelling & packaging

i) Receiving :-

- The prescription should be received by the pharmacist.
- While receiving a prescription ~~should~~ from a patient pharmacist should not change his/her facial expression that gives an impression to the patient that he/she is confused or surprised after seeing the priscription.

ii) Reading And Checking :-

- After receiving the priscription it should be screened behind the counter.
- The priscription is a hospital slip or from a nursing home or from a private ~~prac~~ practitioner and their authenticity should be checked. The signature of the priscriber and the date of priscription is to be checked.
- The pharmacist should read all the lines and words of the prescription. He/she must not guess any word. If ~~their~~ there is any doubt, the pharmacist should consult with the other pharmacist or the priscriber over the telephone.

iii) Collecting & weighing of the material :-

Before companding a prescription all the material required for it should be collected from the shelves or drawers and kept in the left hand side of the balance. After measuring each material should be kept on the right hand side of the balance. After companding the priscription the material. After companding the prescription the material are replaced back into the shelves/drawer where from they are collected.

While companding the level of every containers of

material should be checked thrice in the following manner.
(i) When collected from the shelves/drawer.
(ii) When the material are measured.
(iii) When the containers are replaced back to the shelves/drawers.

iv) Compounding, Labeling & packaging.

- Only one prisciption should be compounded at a time.
- Compounding should be done on a clean table.
- All equipment required should be cleaned and dried.
- The preparation should be prepared according to the direction of the prescriber or as per method given in the pharmacopoeia or formulary and are according to established pharmaceutical art of compounding.
- The compounded medicament should be filled in a suitable container with appropriate lebel depending upon the quantity and use.
- While delivering the prescription to the patient, the pharmacist should explain the mode of administration, direction for use of drugs.

- Sources of Errors in Prescriptions:-

(1) Abbreviation
(2) Name of the drugs — [Digitoxin & Digoxin] ex.
(3) Spength of preparations.
(4) Dosage forms of the drug prescribed
(5) Dose
(6) Instruction for the patient
(7) Incompatibilities

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Posology

It is the branch of science which deal with the medicine dealing with doses of medicaments.

factor Affecting dose of a drug

the following are the some of the factor that influence the dose of a drug.

1. Age :-

Human being can be categorised into the forawing age groups.

a) Neonate :- from birth up to 30 days.
b) Infant :- upto 1 year age.
c) Child in b/w 1 to 4 years.
d) Child in b/w 5 to 12 years.
e) Adult
f) Geriatric (elderly) patients.

In children, the enzyme systems in the liver and renal excretion remain less developed. So, all the doses should be less than that of an adult. In elderly patients, the renal function decline. Metabolism rate also decreases. Drug absorption from the intestine become slower in elderly patients. So, in geriatric patient the dose is less than and should be judiciously administered.

2. Sex :-

Special care should be taken while administering any drug to women during menstruation, pregnacy & lactation. Antihistamic Antihistaminic and sedative drug are not taken during breast feeding because these drug secreted in the milk and the children may consume them.

3. Body Size :-

It influences the concentration of drug in the body. The average dose is calculate for a person with 70 kg body weight (BW). For exceptionally obese (fat) or lean (thin) patient the dose may be calculate on body weight basic.

$$\text{Individual dose} = \frac{\text{Body Weight (kg)}}{70} \times \text{Average adult dose}$$

- Another method of dose calculation is according to the body surface (BSA). This method is more accurate than the body weight method.

$$\text{Individual dose} = \frac{\text{Body surface Area}(m^2)}{1.7} \times \text{Average adult dose}$$

- The body surface Area (BSA) of an individual can be obtained from the following:

$$(BSA)\ m^2 = BW\ (kg)^{0.425} \times \text{Height (cm)}^{0.725} \times 0.007184$$

4. Route of administration :-

In case of intravenous injection, the total drugs reaches immideately to the systemic circulation hence the dose is less in I.V. injection than through oral route or any other route.

5. Time of Administration :- The drug are most quickly absorbed from empty stomach. The presence of food in the stomach delays the absorption of drugs. Hence, a potent drug is given before meal. An irritant drug is given after meal so that the drug is diluted with food and thus produce less irritation.

6. Environmental factors

Stimulant drug are taken at day time & sedative drugs are taken at night. So, the dose of a sedative required in day time will be much higher than at night. Alcohal is better tolerated in winter than in summer.

7. Psychological state

Psychological state of mind can affect the respance of a drug, e.g. a nervas and anxias patient required more general ~~anaesthetics~~ anaesthetics.

Placebo is an inert substance that does not contain any drug. Commonly used placebos are lactose tablets and distilled watar injections. Some time patients often get some physical effect from this placebo. Placebo are more often used in clinical trial of drugs.

8. Pathological status (i.e. presence of disease).

Several diseases may affect the dose of drugs:-

- In gastrointestinal disease like achlorhydria (reduced secretion of HCl acid in the stomach) the absorption of aspirin decreases.
- In liver disease (like liver cirrhosis), metabolism of some drug (like morphine, pentobarbitone etc) decrease.
- In kidney diseace, excretion of drugs (like aminoglycosides, digoxin, phenobarbitone) are reduced, so less doses of the drug should be administered.

9. Accumulation

Any drug will accumulate in the ~~drug~~ body if the rate of absorption is more than the rate of elimination. Slowly eliminated body are often accumulated in the body and often causes toxicity. Eg prolonged use of chloroquin causes damage to retina.

10. Drug interactions :-

Simultaneous administration of two drugs may result in same or increased or decrease effects

Drug administration with dose	Pharmacological effect.
Drug A	Effect A
Drug B	Effect B
Drug A + Drug B	Effect AB

Relationship	Name of the effect	Examples.
Effect AB = Effect A + Effect B	Additive effect	Aspirin + Paracetamol
Effect AB > Effect A + Effect B	Synergistic [potentiation]	Sulfamethaxazole + Trimethoprim.
Effect AB < Effect A + Effect B	Antagonism	Histamine + Adrenaline

11. Idiosyncrasy :-

This is an expectional responce to a drug in few (individual patients).

for examples :- In some patients, Asprin may cause asthma, penicillin causes irritating rashes on the skin etc.

12. Genetic diseases :-

Some patients may have genetic defects. They lack some enzymes. In those case cases some drug are contraindicated.

e.g. Patients lacking Glucose-6-phosphate dehydrogenase enzyme should not be given primaquin (or anti-malarial drug) because it will cause hemolysis.

13. Tolerance

Some times higher dose of a drug is required to produce a given response (previously less dose was required).

→ Natural Tolerance: Some races are inherently less sensitive to some drugs, eg. rabbits & black race (Africans) are more tolerants to atropine.

→ Acquired Tolerance: By repeated use of a drug in an individual for a long time required larger dose to produce the same effect that was obtained with normal dose previously.

→ Cross tolerance: It is the development of tolerance to pharmacologically related drug eg. alcoholics are relatively more tolerant to sedative drugs

→ Tachyphylaxis: (Tachy = fast, phylaxis = protection) is rapid development of tolerance. When doses of a drug are repeated in quick succession an reduction in response occurs — this is called tachyphylaxis. This is usually seen in ephedrine, and also in nicotine.

→ Drug resistance: It refers to tolerance of microorganisms to inhibitory action of antimicrobials eg staphylococci to penicillin.

- Calculations of doses for Infants and Children.

(1) Dose proportionate to Age:

Young's formula: This formula is used for children having age below 12 years.

$$\text{Dose for the child} = \frac{\text{Age in Years}}{\text{Age} + 12} \times \text{Adult dose}$$

- **Dilling's formula:** This formula is used for children having age from 4 to 20 years.

$$\text{Dose for the child} = \frac{\text{Age in years}}{20} \times \text{Adult dose}$$

- **Cowling's formula:**

$$\text{Dose for the child} = \frac{\text{Age in years} + 4}{24} \times \text{Adut dose}$$

- **Freud's formula:** for less than 12 yr of age.

$$\text{Dose for the child} = \frac{\text{Age in months}}{150} \times \text{Adult dose}$$

Examples:

① Average dose = 300 mg

year = 10

$$\text{Child dose} = \frac{10}{10+12} \times 300 = \frac{3000}{22}$$

② therapeutic dose of a drug = 10mg/kg/day.

Patient weight = 156 lb.

how many 250 mg/100 cc → ?

→ Patient weight = $156/2.2$ lb = 70.9 kg.

so, patient needs = 70.9 × 10 = 709 mg of the drug.

three bags needed to be filled of 709 of 250mg bags.

2. Doses proportional to Body weight:

- Clark's formula:

Dose for the child = $\frac{\text{Weight in pound}}{150} \times$ Adult dose.

Dose for the child = $\frac{\text{Weight in kg}}{68.2} \times$ Adult dose.

3. Doses Proportionate to Body Surface Area (BSA).

Dose of child = $\frac{\text{Body Surface Area of child } (m^2)}{1.73\ m^2} \times$ Average adult dose.

- Vetesinary doses: Doses depends upon the type of formulation, age of the patient, sex of the patient, idiosyncracy, drug interaction, body weight, surface area and the severity of the disorder.

Thus as compared to human beings, the doses required for animal are much more higher than human due to high surface area or weight etc.