COURSE CODE: VPC 404
COURSE TITLE: VETERINARY TOXICOLOGY AND PHARMACY
NUMBER OF UNITS: 3 UNITS
COURSE DURATION: TWO HOURS PER WEEK, THREE HOURS OF PRACTICALS PER WEEK

COURSE DETAILS:
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Other Lecturers: Prof. R.O.A. Arowolo, Dr. J.O. Olukunle, Dr. K.T. Biobaku

COURSE CONTENT:
Introduction to toxicology; sources and types of poison, antidotal therapy; toxicology of fungicides, pesticides, herbicides, rodenticides; cyanide, nitrate, nitrite and oxalate poisoning; environmental toxicology; toxicology of heavy metals; plant toxicology; toxins of animal origin; formulation of veterinary drugs; drug prescription, organization and management of a veterinary pharmacy.

COURSE REQUIREMENTS:
This is a compulsory course for all veterinary medical students in the University. In view of this, students are expected to participate in all the course activities and have minimum of 75% attendance to be able to write the final examination.

READING LIST:
INTRODUCTORY TOXICOLOGY; SOURCES AND TYPES OF POISON, ANTIDOTAL THERAPY

Definitions:

- **Toxicology**: It is the science or study of poisons on biologic systems, including their properties, actions and effects. Also their detection and identification, the treatment and prevention of the conditions produced by them.

- **Toxicant**: Any poisonous agent.

- **Toxins/Biotoxins**: Poisons produced by biologic sources e.g venom, plant toxins.

- **Toxicosis/ Poisoning/ Intoxication**: Any disease produced by a toxicant. Could be acute or chronic.

- **Toxicity**: Refers to the amount of a toxicant necessary to produce a detrimental effect.

- **Hazard**: Describes the likelihood of poisoning under conditions of use.

- **Toxicant accumulation/ biomagnifications**: Occurs when absorption exceeds the ability of the body to destroy or excrete a xenobiotic compound.

- **Ecotoxicology**: The study of the relationship of potentially toxic chemicals in living organisms and their environment.

- **Tolerance**: The ability of an organism to show less response to a specific dose of a chemical than it demonstrated on a previous exposure; refers to acquired and not innate resistance.
• LD₅₀: The dose that is lethal to 50% of a test sample or population. Expression of toxicant concentrations is in ppb or ppm in feedstuff, water, air, tissue etc.

**Factors affecting the activity of poisons**

Factors related to exposure:

- Dose
- Duration and frequency of exposure
- Route of exposure
- Time of exposure
- Environmental factors e.g. temperature, humidity etc.

**Biologic factors:**

- Species of animal
- Age and size of animal
- Sex and hormonal factor of animal
- Nutritional and dietary factor
- Health status

**Chemical factors:**

- Chemical nature of the toxicant
- Vehicle/Carrier

**Diagnosis**

- History
- Clinical signs
- P/M lesions
- Laboratory examinations
- Bioassay/Animal inoculation

**Principles of treatment of poisoning:**

- Prevention of further absorption
- Supportive or symptomatic treatment
- Specific antidote
TOXICOLOGY OF FUNGICIDES, PESTICIDES

FUNGICIDE POISONING

- Fungicides are extensively used in industries, agriculture and the home.
- Fungicides vary enormously in their potential for causing adverse effects in humans.
- Many fungicides have low inherent toxicity in mammals and are inefficiently absorbed.
- Examples of fungicides are:
  a. Substituted Benzenes – chloroneb and chlorathanolil
  b. Thiocarbamates – thiram and metam-sodium
  c. Ethylene bis-dithiocarbamates/EBDC compounds – maneb and zineb
  d. Thiophthalimides – captan and captafol
  e. Copper compounds – organic and inorganic
  f. Organomercury compounds
  g. Organotin compounds
  h. Cadmium compounds
  i. Miscellaneous organic fungicides

TOXICOLOGY OF PESTICIDES; ORGANOPHOSPHATES

- A pesticide is any substance or mixture of substances intended for preventing, destroying, repelling or mitigating any pest.
- Pesticides are used extensively as acaricides/ ectoparasiticides in veterinary medicine to control insect pests of both mammals and birds.
- **Insecticides:**
  - Insecticides are a heterogeneous group of chemicals whose desired activity is killing of insects in a very selective and specific manner.
  - Most insecticides are not highly selective and result in poisoning in many nontarget species including man and domestic animals.

On the basis of their chemical nature, insecticides may be categorized as:

- **Organochlorine or chlorinated hydrocarbon insecticides**
  - Dichlorodiphenylethanes e.g. dichlorodiphenyltrichloroethane (DDT), methoxychlor etc; chlorinated cyclodienes e.g. aldrin,
dieldrin etc; hexachlorocyclohexanes e.g lindane; miscellaneous group e.g mirex.

- Organophosphorus insecticides - Parathion, and its oxygen analogue paraoxon, disopropyl phosphorofluoridate (DFP), diazinon, dimethoate, coumaphos etc.
- Carbamate insecticides
- Synthetic pyrethroid insecticides

HERBICIDE AND RODENTICIDE POISONING

HERBICIDE POISONING
- Herbicides are compounds that have the potential of either killing or damaging unwanted plants or weeds.
- The biochemical differences in plants make it possible to design chemicals that have selective toxicity potential against various plants/weeds with no deleterious effects on the crops.

Herbicides are categorized based on their:

A. USES
- Pre-planting herbicides: mixed with the soil before seeding.
- Pre-emergent herbicides: applied before the emergence/appearance of unwanted weeds.
- Post-emergent herbicides: applied after the emergence/germination of crops and unwanted weeds.

B. CHEMICAL NATURE
- Dinitro compounds
- Bipyridium compounds/ Quaternary Ammonium compounds
- Phenoxyacetic acids
- Phenyl or Substituted ureas
- Heterocyclic compounds/Triazenes
- Carbamates and thiocarbamate compounds
- Aromatic/ Benzoic acid compounds
- Chloroaliphatic acids
- Substituted dinitroanilines
C. MECHANISM OF ACTION

- Selective herbicides
- Contact herbicides
- Translocating herbicides

RODENTICIDE POISONING

- Rodenticides are agents which destroy rodent pests such as black rats (*Rattus rattus*) and mice (*Mus musculus*).
- An ideal rodenticide should
  A. Be potent and palatable to the target animals
  B. Not induce bait shyness
  C. Not make the intoxicated animals go out in the open to die
  D. Be specie specific
  E. Cause death in such a manner that surviving rodents will not suspect.

Commonly employed rodenticides are:

- Anticoagulant Rodenticides (Warfarin and Congeners)
  1. α-Naphthylthiourea (ANTU)
     - A selective rodentine
     - Toxic to rats but harmless to human

Mechanism of action:

- Interferes with effective uptake of O₂ from pulmonary alveoli by producing extensive oedema of the lungs due to increased capillary permeability and seepage of fluid into the airways. This leads to formation of froth which further blocks the air passage and the poisoned animal drowns in its own fluid. Dogs and pigs are occasionally poisoned, ruminants are resistant.

Clinical signs:

- Vomiting, hypersalivation, coughing, and dyspnea. Animals prefer to sit.
  Severe pulmonary edema, moist rales, and cyanosis are present. Death from hypoxia may occur within 2-4 hr of ingestion, while animals that survive 12hrs after, may recover.
Post-mortem lesions:
- Pulmonary edema and hydrothorax. Hyperemia of the tracheal mucosa, mild to moderate gastroenteritis, marked hyperemia of the kidneys, and a pale mottled liver are found in most cases.
- Tissue for chemical analysis must be obtained within 24hr.

Treatment:
- Emetics should be used only before respiratory distress is evident. Prognosis is grave when severe respiratory signs occur. Sodium thiosulfate (10% solution) is beneficial.

2. Bromethalin:
- A new non-anticoagulant, single-dose rodenticide, which is a neurotoxin.

Mechanism of action:
- It appears to uncouple oxidative phosphorylation in the CNS. CSF pressure increases, placing pressure on nerve axons, resulting in decreased nerve impulse conduction, paralysis and death. Bromethalin can cause either an acute or a chronic syndrome.

Clinical signs:
- Hyperexcitability, muscle tremors, grand mal seizures, hindlimb hyperreflexia, CNS depression and death may appear ~ 10hr after ingestion. Chronic effects are seen with lower dosage and may appear 24-86 hr after ingestion. This syndrome is characterized by tremors, depression, ataxia, vomiting, and lateral recumbency.
- Bromethalin toxicosis should be considered when cerebral edema or posterior paralysis is present.

Treatment:
- Use of mannitol as an osmotic diuretic and corticosteroids have been suggested, but have shown little effect in bromethalin-poisoned dogs.
- Use of activated charcoal, perhaps for several days, may increase recovery rate.
CYANIDE POISON

Sources of cyanide poison:
- Plants
- Fumigants
- Soil sterilizer
- Fertilizer
- Plants e.g Trigloclin maritims (arrow grass), Hoecus lunatus (velvet grass), Sorghum bicolor, Zea mays (corn), Manihot esculantum etc.

Mechanism of Release of Cyanide and Cause of Toxicity
- The cyanogenic glycosides in plants yield free hydrocyanic acid (HCN) which is hydrolysed by B. glycosidase and hydroxynitrile lyase. The microbial flora and fauna that are inhabitants of the rumen would cause further release, thus discharging the free cyanide.
- The toxicity of HCN is attributed to the high affinity towards metalloporphyrin. The HCN reacts with (Fe$^{3+}$) of cytochrome oxidase resulting in CN-cytochrome oxidase complex. This impairs respiratory electron chain resulting in cytotoxic anorexia and death.

PREDISPOSING FACTORS TO CYANIDE POISONING

1. Soil factors or edaphic factors
2. Season: - cyanogenic glycosides decrease in drought – stricken plants. More at rains or wet season when there are new shoot.
3. Herbicide Sprayer and Fertilizers: Increases the tendencies especially nitrates in phosphorus deficient soils.
4. Feeding on frozen plants may cause a high release of cyanogenic glycosides.
5. Part of the plant eaten - for example in Pyrus malus the poison is more in the leaves and seeds and is less in the fleshy fruit.
6. Species factor: - It is common in large animals such as cattle (ruminants). The monogastrics are less likely to get poisoned.

7. The processing of the material: when silage is not dried, there is increase in toxicity.

**Clinical signs:**

**Acute toxicity:** excitement, lacrimation, hypersalivation, bright red mucosa, nystagmus, death.

**Chronic toxicity:** urinary incontinence

**Differential Diagnosis**

- Nitrate poisoning
- Organophosphorus poisons
- Sulphur poison
- Nitrate poison.

**Diagnosis**

- Appropriate history
- Clinical signs
- Postmortem finding or necropsy
- Demonstration of cyanide poisoning in the rumen using smell “almond smell”.
- Estimating the amount of cyanide in the food.

1. >2000ppm cyanide on HCN is considered very dangerous.
2. 750ppm HCN is considered hazardous
3. 500-750ppm is doubtful
4. <500ppm is considered safe.
5. <100ppm is considered very safe.
TREATMENT

Sodium nitrate 20mg/kg. It could be repeated for 2-4 hours or as needed.

Sodium thiosulphate >500mg/kg I.V. Artificial respiration with oxygen 100% should also be given along with sodium nitrate and sodium thiosulphate.

NITRATE/NITRITE POISONING

Sources:

- Fertilizers
- Preservatives
- Gun powder
- Plants e.g Zea mays, Sunflower, Sorghum, Cereal grasses (oats, millet and rye).

Factors that affect Nitrate poisoning

1. Damp weather condition and cool temperatures of 55°F (13°C).
2. In drought especially when plants are immature.
3. Decreased light, cloudy weather and shading associated with crowding conditions.
4. Edaphic factors: Low soil that is deficient in trace elements like molybdenum and in macro elements like sulphur or phosphorus.
5. Anything that stunts growth increases nitrate accumulation in the lower parts of the plants.
6. Herbicides
7. Nitrates are accumulated in lower stalks but are lesser in leaves and upper stalk.
Clinical signs:

- Weak heart beat
- Subnormal body temperature
- Weakness
- Dyspnoea
- Tachypnea
- Brown or muddy cyanotic, mucous membrane.
- Frequent urination

Treatment of Nitrate poisoning

- I.V. injection of methylene blue in distilled water or isotonic saline should be given at 22mg/kg or depending on severity of exposure. Lower dosage may be repeated in 20-30minutes.

OXALATE POISONING

Sources:

A. Plants e.g Amaranthus retroflexus, Spinacia aleraces, Beta vulgaris, Oxalis spp. Etc.

B. Metabolic synthesis - Formed during the metabolism of ascorbic acid, this forms the insoluble form of the salt.

C. Oxalic acid (ingestion).

Clinical Signs:

- Stomatitis, anorexia, convulsion, dysuria.

Diagnosis:

- History

- Laboratory diagnosis; samples taken are plant or food of animal, urine and blood.

Treatment:
• Lime or calcium hydroxide solution should be given. This reacts with acid to produce insoluble form of calcium oxalate.

• Use menthol or eucalyptus oil to soothe the buccal cavity.

ENVIRONMENTAL TOXICOLOGY

Air Pollution:

1. **Primary air pollutants** – These are pollutants which are directly released in atmosphere in enough concentrations without modifications e.g CO₂, SO₂ and nitrogenous compound (NO, NO₂).

2. **Secondary air pollutants** – The pollutants which interact with each other in presence of certain compounds, particularly energy sources e.g. nitrogenous compounds, ozone, peroxyacetyl nitrate (PAN).

Depending on the chemical nature, two types of pollution are recognized.

   a) Reducing type of pollution – Pollution due to incomplete combustion of coal, fog and cool temperature.

   b) Oxidizing type of pollution or photochemical air pollution – pollution due to hydrocarbons, oxides of nitrogen and automobile exhaust where intense sunlight causes photochemical reactions.

**Carbon monoxide**:

• Is the most notorious and abundant pollutant.

• Larger percentage are from natural sources, particularly combustion of fossil, fuel, atmospheric oxidation of methane, forest fires, terpenes oxidation and ocean microbes.

• CO is highly toxic because it has high affinity for haemoglobin (Hb), thus displaces Hb – bound oxygen and increases carboxy-haemoglobin.

• Dissociation of carboxy-Hb is a slow process this further reduces the availability of oxygen to tissue.
Clinical signs:
* Sweating  * Irritability  * Headache
* Insomnia  * Dizziness  * Blurred vision
* Thirst  * Loss of weight.

Sulphur dioxide:
* Global emission of SO$_2$ is more or less equal from natural and anthropogenic sources.

Natural sources - Volcanoes, decaying organic matter.

Anthropogenic sources – Combustion of sulphur containing coal and smelting of nonferrous ore.
* Sulphur dioxide is readily absorbed on tiny particles of coal and oxidized to sulphur trioxides, sulphuric acid, ammonium sulphate, or other sulphates. The sulphuric acid will come on the earth surface in form of acid rain.

Clinical signs: bronchoconstriction, inflammation of conjunctiva and irritation in the nose and throat.

Hydrocarbons:
* Biochemically, the aliphatic and alicyclic hydrocarbon are generally inert but not to the biological system.
  a) Formaldehyde, other aldehydes ketones, and ozone etc cause irritation to the mucous membrane and system injury as a result of inhalation of aromatic vapour.

Particulate Matter:
This constitutes organic and inorganic particulate materials of different diameters, amongst which are metals and oil. Beryllium and mercury from combustion of coals causes pneumonitis, this is also carcinogenic. Progressively, particles accumulate in the lungs, followed by cessation of clearance epithelium hyperplasia, adenosarcomas and squamous cell carcinoma, particles less than $<5\mu m$ enter tracheo-bronchial tree and irritates the respiratory system.
Nitrogen oxides:
Nitrogen oxide is formed by lightening and microbial digestion of organic matter and by high temperature combustion of cellulose nitrate films.
Nitrogen dioxide is a deep lung irritant and thought to penetrate alveolar capillary membranes where it is converted to nitric acid and produces lung oedema.

Water Pollutants:
Any molecules present in water which are not water and are detrimental to health are termed as water pollutants.

Sources:
Point source- Sewage, industrial units, cooling system, electricity, generating plants.
Non-point sources - agricultural land run offs, containing pesticides, fertilizers, nutrients, phosphorus salinity, acidity.

Types of water pollutants:
  a) Physical pollutants
  b) Chemical pollutants
  c) Biological pollutants

Food Toxicants:
Food of animals and humans contain several naturally occurring substances which are toxic at high concentration. Food toxicants are classified according to their origin:
Fungi, bacterial, environmental contaminants or natural toxin present in plants.

Phytoalexins: Phytoalexins are low molecular weight, antimicrobial agents which are synthesized by plants and are stored in plants after exposure to microorganisms. Other factors which bring about the production of phytoalexins are exposure to bacteria, virus, cold, U-V light, heavy metals, salts, antibiotics, fungicides, herbicides. Some phytoalexins of food plants are:

<table>
<thead>
<tr>
<th>Plants</th>
<th>Phytoalexins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pea</td>
<td>Pisatin</td>
</tr>
<tr>
<td>Soybean</td>
<td>Glyceollin</td>
</tr>
<tr>
<td>Bean</td>
<td>Phaseollin</td>
</tr>
<tr>
<td>Rice</td>
<td>Oryzalexins</td>
</tr>
<tr>
<td>Castor bean</td>
<td>Casbene</td>
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<tr>
<td>Carrot</td>
<td>Falcarinol</td>
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</tbody>
</table>
Toxicants of animal origin:

Drugs and chemicals are used in animals not only for prevention and treatment of disease but also for promotion of growth. Residues of antibiotics, other drugs or pesticides in milk, meat or eggs of animals and birds have been detected.

Radiation Hazards and Toxicity

- Radiation is produced through decomposition or disintegration of an unstable naturally or synthetic element.
- Radioactive materials are being increasingly used in medicine, industry, agriculture and power generating reactors.

The sources are as follows:

a) Natural Sources.

b) Anthropogenic sources.

Natural Sources: Cosmic rays from space and external terrestrial radionuclides composed mainly of the emission from Uranium and Thorium in geo-chemical environment consisting of certain rocks, soil and phosphate deposits. Other natural sources are of radiation are potassium$^{40}$, rubidium$^{87}$, hydrogen$^{3}$, carbon$^{14}$.

Anthropogenic Sources: Nuclear reactors that contain radio active substances contaminate pasture and fields.

Mechanism and Pathogenesis: Radiation toxicity represents a dynamic interaction with matter by direct or indirect processes to form ion pair, some of which are free radicals. The free radicals interact with macromolecules that make up the organelles of the cell. This cause damages to the D.N.A strands to cause breakage point mutation and chromosomal aberrations with the subsequent loss of those gene products coded for by that portion of D.N.A. If the code is required for the cell to maintain life, the cell looses its physiological and structural functions and this result to death.

Types of Radiation Toxicity

i) Acute toxicity

ii) Subacute toxicity

iii) Chronic radiation toxicity
HEAVY METALS POISONING IN ANIMALS

“Heavy Metals” are chemical elements with a specific gravity that is at least 5 times the specific gravity of water. There are 35 Metals that are of concern because of occupational or residential exposure, 23 of these are heavy elements e.g antimony, arsenic, chromium, cobalt, copper, gallium, gold, iron, lead, mercury, nickel, platinum, silver, tellurium, thallium, tin, uranium, vanadium, and interesting, small amounts of these elements are common in our environment and diet and are actually necessary for good health, but large amounts above the average body trace quantity requirement would predispose to toxicity.

Arsenic Poisoning

Factor that affect arsenic poisoning

- Oxidation state of arsenic
- Solubility
- Species
- Animal Involved
- Duration of exposure.

Sources of poisoning: Poisoning occurs due to arsenic trioxide, arsenic pentoxide, sodium and potassium arsenite.

Toxicokinetics

After absorption, arsenic is distributed throughout the body but tends to accumulate in the liver and kidneys.

- Pentavalent arsenic is metabolized to trivalent.
- In domestic animals, arsenic does not stay in soft tissues for long period. It is rapidly excreted in bile, milk saliva, sweat and urine and faeces
- After chronic exposure the poison stays in bones, skin and keratinized tissues such as hoof, hair.
- Arsenic does not cross the blood brain barrier.
- Milk that is poisoned by arsenic can be toxic to humans.

Clinical Signs:

Acute: Profuse diarrhoea, severe colic, dehydration, weakness, depression, weak pulse, cardiovascular collapse.

Peracute: Animals are found dead.
**Subacute cases:** The animal may live for several days signs include colic, anorexia, depression, staggering, weakness, diarrhea, with blood and mucosal shreds.

**Chronic:** Are rare and are characterized by wasting, poor condition, thirst, brick-red mucosal membrane, normal temperature and a weak and irregular pulse.

**Differential diagnosis**
- Caustic poisoning
- Irritant paint poisoning
- Urea chlorate
- Pesticides poisoning
- Lead poisoning

**Treatment**
- Administration of G.1 protectants e.g. charcoal, kaolin-pectin
- Supportive fluid therapy
- Administration of BAL (Dimercaprol) at 4-5mg/kg, deep intramuscular
- D-Penicillamine 10-50mg/kg, orally tid or qid for 3/7or 4/7.

**Lead**

In Veterinary Medicine, lead is one of the most common causes of metallic poisoning in dogs and cattle. Only 1-2% of the ingested lead may be absorbed. The organic form of lead could penetrate intact skin. Organic forms are tetraethyl lead and tetramethyl lead.

**Sources of poisoning**
- Curious animals may ingest lead-based paints.
- Lead tetraoxide, carbonate, or sulphate
- Engine oil and lead battery improperly disposed
- Feeding animals with feed that was sprayed with lead insecticides (lead arsenate).

**Toxicokinetics**
- Lead salts are sparingly soluble
- Absorption of lead from GIT is very limited (1-2%) and therefore about 98% of lead is eliminated in faeces.
Clinical Signs: In cattle, GIT and nervous signs after 24 hours of exposure to toxicity blindness, salivation, spastic twitching of eyelid, jaw champing, tremor convulsion.

Differential diagnosis:
- Polioencephalomalacia
- Nervous coccidiosis
- Tetanus
- Hypovitaminosis A
- Hyomagnesemic tetany
- Insecticide poisoning

Treatment
- Magnesium sulphate 400mg/kg per os
- Barbiturates tranquilizer may be useful to control convulsion
- Calcium disodium edentate given intravenously or subcutaneously at 110mg/kg bid for three days.
- D-Penicillamine can be administered orally at 110 mg/kg/day for two weeks
- Calcium borogluconate I.V recommended at 250-500mg/kg.

Other heavy metals are Mercury, Manganese, Aluminium etc.

SOME TOXIC PRINCIPLES IN PLANTS

A toxic plant may be defined as “one which detrimentally affects the health of a man or animals when eaten in such amount as would be taken normally or under circumstances like restriction of choice of diet or extreme hunger”.

A plant is termed a toxic plant when through contact or ingestion hinders or destroys normal processes leading to distressing symptoms, pathology or mortality.

The toxic (active) principles present in the plants are called as phytotoxin. The toxic principles or phytotoxins are as follows:

a) Alkaloids
b) Terpenes
c) Glycosides
d) Organic acids
e) Resins
Alkaloids
Chemistry:

- They are basic nitrogens substances containing cyclic nitrogen.
- They are insoluble in water.
- Most occur in combination with plant acids.

Toxic alkaloids examples – Tropane (atropine like), pyrrolizidine alkaloids. Pyridine, quinolines, isoquinolines, Indole, quinolizidine, steroidals alkaloids, phenylamine.

Terpenes
Chemistry:

- They are 5-carbon skeleton of isoprene.
- They are classified on basis of number of isoprene.
  1. Monoterpenes e.g. canthandine (C10 compounds).
  2. Sesquiterpenes (C15 compounds).
  3. Diterpenes (Aconitum sp.)

<table>
<thead>
<tr>
<th>Type of terpenes</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Monoterpenes</td>
<td>Canthardine,</td>
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<tr>
<td></td>
<td><em>Anamirta cocculus</em></td>
</tr>
<tr>
<td>Sesquiterpenes</td>
<td><em>Coriaria myrtifoli</em></td>
</tr>
<tr>
<td>Diterpenes</td>
<td><em>Aconitum sp</em></td>
</tr>
<tr>
<td>Terpenes</td>
<td><em>Lantana sp</em></td>
</tr>
</tbody>
</table>

Glycosides
Chemistry:

- The compounds are ether-like combinations of sugars with other organic structures.
- When two parts of the molecules are connected, they are non-active.
- But when two parts are separated from sugar moiety, they are active. E.g. aglycone, genin. The separation of aglycone becomes active to cause toxicity.

Proteinaceous Compounds
The proteinaceous compounds are harmless and often beneficial agents.
After ingestion, protein get hydrolysed through various enzymatic reaction in the gastrointestinal and amino acids are absorbed into the system for protein synthesis in the body.

<table>
<thead>
<tr>
<th>Type</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>Abrin from <em>Abras precatorius</em></td>
</tr>
<tr>
<td></td>
<td><em>Ricinus communis</em></td>
</tr>
<tr>
<td>Polypeptides</td>
<td>Amatoxins, phallotoxins, <em>Amanita sp.</em></td>
</tr>
<tr>
<td>Amines</td>
<td>Aminotryptaline from seed of <em>Sativas odoraties, phoradendron sp.</em></td>
</tr>
<tr>
<td></td>
<td>imosine from <em>Mimosa pudica.</em></td>
</tr>
</tbody>
</table>

**Organic acids**

Chemistry:
These are mostly acids that are accumulated by the plants especially in their fruits e.g. malic acid, tartaric acid, citric acid or ascorbic acid.

**Resins and Resinoids:**
Toxic plants are phenolic compounds. One of the most important naturally occurring phenolic resins in plants is tetrahydrocannabinol (THC) and related compounds from *Cannabis sativa* (marijuana or hemp). Other examples are poison ivy, poison oak hypericin from *Hypericum perforatum*.

**Some poisonous plants in Nigeria:**
Plants containing cyanogenic glycosides: *Manihot esculenta* (cassava), *sorghum bicolor* (Guinea corn), *Phaseolus lunatus* (Lima beans) and *passiflora foetida* (Stinking passion flower).
The toxicity signs associated with these plants are: respiratory paralysis, excitement, convulsions and ultimately depression, peripheral neuropathy of optic nerves leading to blindness.

**Plants containing Neurotoxic alkaloids:**
Physostigmine, scopolamine, atropine nicotine, solanine, pyrrolizidine alkaloids and strychnine. Physostigmine is obtained from ordeal bean of Calabar or *Physostigma venenosum*.
Strychinine Containing plants
Strychinine from species of Strychnos used as rodenticide, causes violent vomition and convulsion through inhibition of spinal cord reflexes to produce extreme hyper sensitivity and tetanus-like, spasm.

Plants Present in Nigeria that predispose to photosensitization
Hepatogenous photosensitisation causing plants induce signs of C.N.S disturbances. Plants that are incriminated are as follows: Gossypium spp., Pteridium aquilinium or Bracken fern is associated with convulsion, incoordination, paralysis, opisthotonus, death.

Aflatoxins - Aflatoxins are toxic substances from metabolic processes of toxigenic fungi Aspergillus flavus and A. parasiticus. Aflatoxins are produced in varying quantities in a variety of grains, nuts, cotton seed meal, maize meals, wheat barley, oats and other cereals.

The most toxic Aflatoxin:  Aflatoxin B₁ (AFB₁) while B₂ and G₂ are present in less concentration.

Toxicity order: B₁ > G₁ > B₂ > G₂.
The β toxins closely related with structure of pyrroloidone. The β toxins are carcinogenic, teratogenic and hepatotoxic.

Clinical signs: Aflatoxicosis may be acute, sub acute or chronic.
Acute toxicity: The dose of 4mg/kg of aflatoxins cause death of sheep, claves and pigs within 15 – 18 hours due to hepatic insufficiency. Clinical signs include anorexia, depression, ataxia, dyspnoea, anaemia, haemorrhages, bloody faeces, tremors, convulsions and death.

LD50 values of AFB₁ in some species

<table>
<thead>
<tr>
<th>Species</th>
<th>LD50 value (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbits</td>
<td>0.3 - 0.5</td>
</tr>
<tr>
<td>Ducklings</td>
<td>0.5</td>
</tr>
<tr>
<td>Cats</td>
<td>0.3 – 0.6</td>
</tr>
<tr>
<td>Dogs</td>
<td>0.5 – 1.0</td>
</tr>
<tr>
<td>Cattle</td>
<td>0.5 – 2.0</td>
</tr>
<tr>
<td>Horses</td>
<td>&gt;2.0</td>
</tr>
<tr>
<td>Chicken</td>
<td>&gt;2.0</td>
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</table>
Sub-acute toxicity
Consumption of sub lethal concentrations of aflatoxins for several days or weeks causes this condition which is characterized by symptoms of icterus, hypoprothrombinemia, haemorrhages and haematomas.

Chronic toxicity
Chronic aflatoxicosis is the most commonly occurring syndrome in domestic animals and birds. The obvious signs of toxicity might begin in 1-2 months with decrease in feed efficiency, weight gain, productivity, icterus, ascites, oedema of lungs and abortion in pregnant animals. Death had been reported in ponies following AFB₁ feeding at 0.075mg/kg per day. 26 – 32 days after 0.15mg/kg/day.

Differential diagnosis
i) Warfarin poisoning
ii) Copper poisoning
iii) Carbon tetrachloride
iv) Pyrrolizidine
v) Infectious hepatitis.

Prevention and treatment
i. Contaminated feed must be withdrawn immediately.
ii. Provide easily digestible low fat and high protein diet/feed.
iii. Supportive therapy with multivitamins.
iv. 0.5% hydrated sodium calcium aluminosilicate as feed additive in the feed of pigs and lambs.
v. Anabolic steroid stanozolol 2mg/kg by I.M. injection at 4-5days.
vi. Activated charcoal at 6.7mg/kg intraruminally as 30% w/v
vii. Oxytetracycline (10mg/kg, I.M. once daily).
viii. Intravenously administered quantities of 5% dextrose.
ix. Supplement diet with hepatotonics
x. Administer antioxidants.

Ergot poisoning:
Ergot is a parasitic fungus (Claviceps purpurea), which invades the flowers and spikelets of cereals, particularly rye, oats, barley, wheat and grasses.
Ergotism commonly occurs in cattle, sheep, and others.
Ergot contains a number of pharmacologically active alkaloids namely, ergometrine, ergotoxin, ergocornine, ergocristine, ergocryptine.

**Toxicity (Ergotism):** Generally, animals may show lameness, irregular gait and evidence of pain in the feet and the posterior extremities being chiefly affected as early as within 10 days.

**Treatment**
- No specific antidote is there.
- Offending feed should be immediately withdrawn.
- Provide a warm, clean and stress free environment.
- Give symptomatic treatment.
- Oral purgatives (magnesium sulphate).
- Broad spectrum antibiotics

**Gossypol poisoning**
Gossypol, the predominant pigment and (Gossypium spp) and other polyphenolic pigments are contained within small discrete structure called pigment glands found in various parts of the cotton plant.

**Clinical findings:**
Signs may relate to effects on the cardiac, hepatic, renal, reproductive, or other systems. Prolonged exposure can cause acute heart failure. Reproductive effects include reduced libido with decreased spermatogenesis and sperm motility.

**Treatment**
- A high intake of protein, calcium hydroxide, or iron salts appears to be protective in cattle.

**TOXINS OF ANIMAL ORIGIN**
- Toxins of animal origin are compounds or enzymes of definite animal species (terrestrial or marine).
- Venomous animals are classified into actively venomous and passively venomous.
Venoms of bees, hornets and wasps

- The high mortality rate from stings of these animals is attributed to anaphylactic shock resulting from hypersensitivity to venom peptide. They have highly specialized apparatus which serves for secretions, storage and ejection of venom. Composition of Hymenopteran Venom is biogenic amines, peptides and small proteins, and kinins.
- Mortality is higher with bee toxins than snake venom. Bee toxin causes desensitization leading to allergy, anaphylactic shock and death.

Treatment of bee and wasp poisoning

a. Removal of sting if available
b. Bee stings should be washed in alkaline e.g. soap solution or dilute NH₃. Wasp stings are bathed in dilute acid (vinegar)
c. Use of antihistamine e.g. promethazine.

SNAKE VENOM

- Quantity of venom ejected depends on size and species of snake.
- Composition of snake venom includes protein and non-protein constituents.
- Actions of snake venom are classified into primary effects and secondary effects.
- Of all animals, dogs by far suffer from snake bites as dogs frequently attack snakes and are bitten on the neck or head. Cats tend to avoid snakes and they appear resistant to snake venom.
- In decreasing order, the sensitivity to snake venom is horse, sheep, ox, goat, dog, pig and cat.

CLINICAL SIGNS:

HYDROPHEID ENVENOMATION (WATER SNAKES)

- The assaulted animal senses no pain except for the initial prick. Thereafter, it develops muscular stiffness, lockjaw followed by generalized flaccid paralysis. Terminally, there is myoglobinuria, urine and fecal incontinence, sweating and respiratory failure.

ELAPIDAE ENVENOMATION

- Pain at site followed by numbness, lassitude, drowsiness comparable to alcohol intoxication followed by a sense of slight respiratory difficulty, weak pulse,
tachycardia, drooping of eyelids, difficulty in bellowing, paralysis of bronchial and laryngeal muscle, coma, cessation of respiration and death.

VIPERIDAE AND CROTOLIDAE ENVENOMATION

- Burning piercing pain at the site of wound, edema, lymphaginitis and regional lymphadenitis. As time progresses, there is petechial formation, subcutaneous gesticulation and hematoma at the region of bite. Diffuse haemorrhages resulting in epistaxis, hematemesis and haematuria. Neurotoxic activities are seen with vagal paralysis, weakening of accommodation.

DIAGNOSIS

- Presence of fangs marks which are seen in the centre of a swollen area.

TREATMENT

The most important is the speed of action taking towards the treatment. First aid is important.

1. Application of a tourniquet though its use is doubtful in case of vipers which induces local edema.
2. Incision and suction - Incision should be small and suction should be by cupping. Mouth suction carries the risk of envenomation.
3. Life saving treatment
   a. Use of the correct antivenin obtained from the horse immuned against the correct snake. Problem of identifying a correct snake.
   b. Polyvalent serum administered IM or IV for serious cases.
   In case of vipers some of the serum has to be infused around the bites.
   Cortisone and similar steroids increase the survival rate and enhance the action of the serum and should be combined only with polyvalent serum.
4. Introduction of saline and calcium borogluconate is also useful.
5. Pethidine is adequate for alleviating pains
6. Antibiotic therapy may be required in cases of suspicion that fangs are contaminated.
7. Horses normally show edema of the throat and nasal region when bitten on the head and this may necessitate tracheotomy.

SCORPION VENOM
- Unlike snakes, all scorpions are venomous. The venom is injected by means of a stinger found at the tip of the telson, the terminal structure of the tail.

CLINICAL SIGNS
- Pain, local edema and fever 1-20 hours after sting, sweating, pallor, restlessness, anxiety, salivation, nausea, abdominal cramps. Sensation of choking, muscle weakness and twitching. Initial tachycardia changes to bradycardia and initial hypertension to hypotension. There is respiratory distress and subsequent cyanosis. Death results from cardiovascular collapse and pulmonary oedema.

TOAD TOXIN
- The cutaneous secretion contains toxins called bufotoxin and bufogenin.
- The bufotoxins have adrenalin-like effect. The bufogenin called bufodienolides, in structure have digitalis-like action.

TREATMENT
a. Wash the area
b. Treatment with atropine which is a specific antagonist
c. Sedation with sodium pentobarbitone
d. Administration of an analeptic to counteract depression eg laptazol
e. Artificial respiration.

SPIDER VENOM - Black widow spider (Lactodectrus mactanus)

CLINICAL SIGNS
- Extreme pain, emesis, rigidity abdominal muscles, jelly like oedema at region of bite, weakness, dyspnoea followed by paralysis. In acute cases, death occurs in 4-6 hours.
- Spider bites are differentiated from snake bites by the absence of fang marks.

TREATMENT
- If specific antivenim is not available, then an IM injection of serum of an immuned dog could be used.
• Give analgesics to relieve pain.

FISH TOXINS
• About 40 spp of round fish are known to be poisonous. Most belong to the family Tetroodontidae. Their toxins are tetrodotoxins which are concentrated in the ovary, liver and to some extent in the intestine and skin. Some species also have their muscles being toxic. Toxicity relates to specific toxin inherent to the fish.
• The shell fish produces saxitoxin whose mechanism of action is qualitatively similar to that of tetrodotoxin.

Mechanism of action of tetrodotoxin
• There is selective inhibition of cellular Na ion movement. Effect of tetrodotoxin is 100x more then that of cocaine and so tetrodotoxin can be used as local anesthetic.

FORMULATION OF VETERINARY DRUGS

Drug Formulations
• Pharmaceutical preparations of a drug.
• Compounded to provide convenient means of administering a dose of the drug.
• Provide accurate and reproducible dosage.
• May be designed for oral, parenteral or topical application.
• Entails mixing of active ingredient with a variety of excipients e.g starch (for tablets), lactose (for capsules or tablets), solvents (for liquids and injectables), preservatives, coloring agents etc.

Formulations and Drug Therapy
• Similar formulations containing the same amount of active compound do not necessarily elicit the same therapeutic response.
• Formulation processes influence the release rate of drug from dosage forms e.g high compression force increases hardiness (mechanical resistance) of tablets.
• Changes in drug release rate from a formulation changes absorption rate, bioavailability and plasma concentration versus time profile.
Parameters Used to Compare Drug Formulations

- Chemical equivalence: refers to identical dosage forms which contain identical amount of the same chemical substance and meet the physicochemical standard of the Pharmacopoeia.
- Biological equivalence: a condition attained when chemically equivalent dosage forms administered in the same amount provide the same biological or physiological availability which can be determined by measuring plasma or tissue levels of the drugs.
- Clinical equivalence: a condition attained when two chemically equivalent dosage forms administered in the same amount provide the same therapeutic effect as measured by the control of symptoms of a disease.

Factors influencing choice of Drug Formulation

- Nature of the disease (acute, chronic)
- Site of the disease (systemic, local)
- Physicochemical properties of the drug (volatile?)
- Chosen route of administration

Classes of Drug Formulations

1. Immediate release e.g tablets, ointments, aerosol etc
2. Controlled release e.g subdermal implants etc

Immediate Release Drug Formulations

Solid Dosage Forms:

Tablets

- A mixture of active drug and inert binding materials or excipients, usually in powder form, pressed or compacted into a solid.
- Some tablets are in the shape of capsules, and are called “caplets”

Wettable Powder

- Drug dosage form in fine particles.
- Could be sprinkled on feed or dissolved in drinking water.
- It is commonly used in poultry.
Suppository
- Inserted as a solid into the rectum (rectal suppository), vagina (vaginal suppository) or urethra (urethral suppository), where it dissolves inside the body to deliver the drug.
- Used to deliver both systemically-acting and locally-acting medications.

Capsule
- Hard gelatin e.g ampicillin capsule for dry, powdered ingredients or miniature pellets.
- Soft gelatin e.g garlic capsule.
- Primarily used for oils and for active ingredients that are dissolved or suspended in oil.

Semi solid Dosage Forms:
- Examples are ointments, creams and gels commonly used to treat dermatological diseases.
- Ointments are homogeneous, viscous, semi-solid, greasy, thick oil, intended for external application to the skin or mucous membranes.

Liquid Dosage Forms:
Suspension
- Formulation of two-phase system composed of a finely divided solid that is dispersed in a liquid phase, which is usually water.
- Suspensions are common as oral drug preparations.
- Never administer intravenously.

Emulsion
- Aqueous suspension of insoluble liquid substance usually with emulsifying agent to stabilize the preparation.
- Usually administered orally or topically.

Solutions
- Oral Solution: Aqueous preparation of drug for oral use. The drug is in true solution.
• **Parenteral Solution:** Sterile and pyrogen free aqueous preparation for injection. Drugs may also be dissolved in oil for prolonged absorption.

• **Ophthalmic Solution:** Sterile hypotonic aqueous solution of drug for administration into the eye.

**Tinctures**

• Tinctures vary in strength. Examples are tincture of iodine, opium, belladonna and digitalis.

**Liniment**

• Liquid preparation of a drug in which the drug is dissolved or suspended in dilute alcohol or water. They often contain dissolved or emulsified oils and are applied to the skin by rubbing or massage.

**Lotion**

• Usually an oil in water base which contains insoluble medicinal agents in suspension and is applied to the skin without rubbing following which the solvent evaporates leaving a film of drug.

**Aerosol**

• The drug exists as liquid or solid particles so small as to remain suspended in air for long periods.

• Aerosol generators may produce particles in 1-5µm ranges.

• For therapeutic purpose, aerosols are introduced in the body by inhalation.

**Controlled-Release Drug Delivery Systems**

**Synonyms:** Sustained; Modified; Prolonged; Slow; Gradual and Extended Forms

• Provide an initial therapeutic dose immediately following administration and subsequently followed by a gradual release of the drug over a prolonged period of time.

• Extend the duration of pharmacological response compared to the conventional single dose formulation.

• They produce therapeutic blood level quickly and maintain such levels without the usual “peak –and-valley” effect of a normal dosage form.

• Examples: enteric coated tablets, sub dermal implants, depot antibiotics etc.
Advantages:
- prolonged absorption
- reduced peak blood concentration so side effects associated with peak blood levels are minimized
- predictable and reproducible drug release kinetics
- premature inactivation and elimination of the drug is avoided
- extended and regular pattern of therapeutic effects
- extended duration of drug action
- reduced frequency of drug administration and animals restraint
- improve compliance
- targeting of drugs to specific sites and selectivity of action is possible

Disadvantages:
- Toxicity may result if actual release rate becomes high (large doses are given at once, it being assumed that there will be slow but continuous release of drug from the formulations).
- A reduction in the expected rate of release may result in therapeutic failure.

DRUG PRESCRIPTION ORDER

Prescription Order-Definition
- A written instruction by a veterinarian to a pharmacist for issuing medical preparations for a patient.
- It primarily states what is to be given; to which animal; how much; how often; which route; how long; and by who?
- It is a legal document.

Prescription Writing in Vet Practice
- Veterinarians seem to be more adept at dispensing rather than prescribing drugs.
- Level of veterinary practice is such that the practicing vet depends on profit from the dispensing and sale of drugs.

Reasons Why Veterinarians Should be Proficient In Writing Prescription Order
- The vet can charge just about the same fee as when drugs are dispensed.
- Writing a prescription reduces the investment tied up in drug inventory.
• Prescribing provides the vet with a supply of pharmaceuticals that might not always be available on the shelf of the clinic.

• If a client does not pay his/her bills, the cost of the medicines prescribed is not lost.

• Clients are more likely to pay for two smaller fees than one large fee.

**Types of Prescription Order**

Pre-compounded:

• Prescription of drugs in fixed dose combinations prepared by pharmaceutical industries.

• Dispensed without further alterations.

• Simple but drug dosage cannot be manoeuvered to suit clinical conditions.

• Now used commonly.

Extemporaneous or compounded:

• The Veterinarian selects drugs, their doses and formulations to be made and then instructs the pharmacist to compound the medicine.

• Selections and doses can be made to suit clinical conditions.

• Not common nowadays.

**What To Avoid in Prescribing Drugs**

• Prescribing a drug without demonstrated efficacy.

• Prescribing a drug with inherent hazard that is not justified by the seriousness of the disease. This is sometimes referred to as ‘heroic’ measures.

• Prescribing drugs in inadequate amounts and for inadequate periods.

• Simultaneous use of more than one drug without consideration for interaction.

• Prescribing drugs without consideration for cumulative effect.

• Prescribing of needlessly expensive drug.

**PRESCRIPTION ORDER WRITING**

**Rules of Prescription Writing**

• Language of the prescription is English with some Latin abbreviations.

• The use of Latin phrases has become obsolete.

• Official/Generic names of drugs are preferred.
- Trade or proprietary names may be used but these restrict the pharmacist who must supplies the drug to the specified name.
- Substitution of one therapeutic agent for another is not permitted even if the two drugs are considered pharmacodynamically equivalent e.g NaHCO₃ for Mg trisilicate.
- If the vet prefers a particular product but is unsure of its availability, he/she could insert the trade name in bracket after the official name e.g acetylsalicylic acid (Bufferin®).
- Write “Brand Necessary” on the prescription if you insist on the particular product.

**Metrology in Prescription**

- Metrology is the study of weights and measures.
- The metric system is used exclusively now in expressing drug weights.
- Drug weights are measured most commonly in milligrams.
- Dosages are expressed as x mg of drug A per kg of body weight of animals.
- Concentrations of liquid preparations are expressed as x mg of drug A per ml.
- Dosages of drug administered in feed or water may be expressed as parts per million (ppm).

**Parts of A Prescription Order**

**Superscription:**

- Practice name and address: This may appear before or after the prescription.
- Date of prescription: This is essential for record purposes and it also enables the pharmacist to detect submission of old prescription order.
- Name and address of the client
- Identification of the animal
- The symbol, partly from the Latin word ‘recipe’ meaning ‘take thou’

**Inscription:**

- Drug Name
- Dose=Quantity of drug per dose form
- Dose Form = The physical entity needed, i.e tablet, suspension, capsule
Clarity of number - 0.2, 20 not 2.0 (zeros lead but do not follow)

Subscription:
- This is the doctor’s instruction to the pharmacist as to what the pharmacist is to do with the ingredients i.e.
- the type of pharmaceutical preparation to be made
- the quantity or number of packs to be dispensed.

Signature or Transcription:
- This is the directive to the pharmacist as to what details should appear on the label as directive to the animal owner or patient (in human medicine).
- The instructions contained in the signature usually encompass the amount of drug to be taken, the frequency of the dose, route of administration and other factors.
- It is linked to the Latin word ‘sigma’ meaning ‘write’, ‘mark’ or ‘label’.

Refill information
Prescriber’s signature and qualification.

**Inscription protocol**
- Avoid abbreviation
- Write the name of each drug on a separate line
- Capitalize the first letter in the name of each drug or ingredient

**Subscription protocol**
Subscription is usually a short sentence e.g.
- Make a solution
- Mix and place in 10 capsules
- Dispense 10 tablets

Subscription could also be a word e.g. “Mix” which may be written as ‘M’ an abbreviation from the Latin word ‘.misce’ meaning mix.

**Signature or Transcription Protocol**
- The directives are preceded by the abbreviation ‘Sig’ or ‘S’ ‘Label’ e.g
  Sig. For animal treatment only. Apply calamine lotion daily to skin lesions on horse No MNO 734.
- The signature is usually written in English but several Latin phrases and abbreviations are inserted.
The pharmacist usually translates these abbreviations and label the client’s medicine accordingly e.g. 1 cap tid, pc. Meaning 1 capsule 3 times daily after meals.

Express dosages as mg/kg and the frequency of administration in hours such as q4h (every four hours) rather than tid.

**write**
- ‘take’ for those preparations designed for internal use
- ‘apply’ for ointment or lotion
- ‘insert’ for suppositories
- ‘place’ for drops.
- Never write “take as directed” i.e. do not give a verbal directive.
- The intended purpose of the prescription can be stated e.g. ‘for relief of pain’ Doing so reduces chances of errors.

The label should also contain
- The drug(s) and strength
- Special instructions (shake well, refrigerate etc).
- Warnings

### ORGANIZATION AND MANAGEMENT OF A VETERINARY PHARMACY

**Objectives:**
- Maintain a permanent stock of drugs and appropriate medical supplies.
- Reduce costs of procurement and manage wastage.
- Save time and optimize the work of the members of staff.
- Easier to continuously evaluate consumption of drugs and medicaments.

**Choice of drugs:**
- Use the National Essential Drug List (drugs selected based on national requirements and drug policy).
- Medical items (materials for sterilization, injection, suture) should also be limited to the essentials and a standard list prepared.
Advantages of using the Essential Drug List
- Better therapeutic management due to more rational and safer use of a restricted number of essential drugs.
- Economic and administrative improvement at the level of purchase, storage, distribution and control.

Designation of drugs
- Use International Nonproprietary Name/Generic Name (INN) as exist in all standard lists.

Classification of drugs
Pharmaco-therapeutic classification:
- Drugs are grouped according to their therapeutic action.
- In some cases, a drug can appear in several groups.
- Easier to insert supplies from different origins as well as find a substitute for a missing product.

Alphabetical classification according to routes of administration:
Drugs are divided into four groups namely
- Oral drugs
- Injectables
- Infusion solutions stored separately because of their bulk
- Drugs for external use and disinfectants
- Smaller medical materials classified in sub-categories: dressing, injection, suture.

Drugs are then listed in alphabetical order within each group.
- This satisfies the criteria of simplicity and standardization needed for the whole management system.
- Non specialized personnel can work with it.

Note:
- Use whichever classification is adopted at every level of the management system (ordering, storage, distribution, dispensing) in order to facilitate all these procedures.
ARRANGEMENT OF MEDICINES AND MATERIALS

- Arrange stock according to the classification adopted.
- Every product should have its own well defined place shown by a large label giving the name of the product in INN, its form and dose; for example; Ampicillin caps 250mg.
- Narcotic drugs such as fentanyl, pethidine, morphine should be kept in a locked cupboard.
- Label the box and bottle of every drug correctly and clearly with the name of the product in INN, the dose, the form, the expiry date.
- Arrange the products with the ones with the latest expiry date at the back of the shelves and those that should be used first in the front.
- This arrangement is essential to avoid products extending pass their expiry dates and becoming unusable.

Storing bulky material

- Put a few boxes in their normal place and, on the label, state where the rest of the stock is kept.
- Do not separate the rest of the stock in several places.

Storing medical materials

Because of the diversity of the articles to be stored;

- It is preferable not to use a strict alphabetical ordering.
- Group the articles by category e.g injection material, dressing, sutures.
- Allow enough space for each drug
- The arrangement should make it possible to work “by sight”.
- It should be possible to pick out the number of boxes of each product.
- In a few minutes, it should be possible to work out how many weeks or months stock of a given product remains.
- An empty space behind a label immediately shows that the product is out of stock
- A few hours should be enough to do a complete stock inventory

A list of the commercial names and the corresponding INN can be put up

- to enable a person who is not familiar with the INN system to find their way around in times of emergency
- in case of sudden replacement
- in order to train the auxiliary staff

Management of the Pharmacy

Stock-control

Stock Cards - 1

- Main instrument for stock-control.
- For each item (drug and material), a stock-card is made out and regularly updated, preferably by the same person.
- These cards allow
  - the identification of all movements of stock, in or out
  - the theoretical stock level to be available at any time
  - the consumption of the different users to be monitored
  - the orders to be correctly foreseen
  - an assessment of what and how much has been lost (difference between the theoretical stock and the actual stock after inventory)

Stock Cards - 2

The following can be noted on the stock-card

- The name of the product in INN, the form and the dose
- All the movements (entries, exits, origin, destination) and the date
- Orders made and the date
- Inventories and the date
- Safety stock
- Maximum stock
- Other storage areas for this product
- Unit price
- The quantities are always recorded in units (e.g. 5,000 tablets, 80 ampoules) and never by box (10 boxes of ampicillin tablets could corresponds to 200 tablets (10 boxes of 20 tablets) or 10,000 tablets (10 boxes of 1,000 tablets).
Stock Cards – 3

- Write only one movement on each line, even if several operations take place the same day.
- When an order is made, the date, supplier, and amount ordered are recorded. The stock column is not changed. When the order arrives, the amount received is included in the “incoming” column, and the “stock” column is then modified.

Calculations of Stock Levels

Monthly consumption:
- Calculated from the exit recorded on the stock cards.
- Add the quantities in the outgoing column from several months (3, 6 or 12) and divide the total by the number of months.

Working stock:
- Working stock corresponds to the amount of each drug consumed between supplies.
- For example, if the supplies arrive every three months, working stock = monthly consumptions x 3.

Safety stock (or reserve stock):
- This is the quantity below which the stock should never fall at the risk of running out of stock. This stock is planned to compensate for any delays in delivery, increases in consumption or possible losses.
- It depends on the delivery time of the orders.
- The quantity to be kept as a safety stock is generally calculated as half of the consumption during the time between two deliveries.
- It considers the risks of running out of stock and having drugs pass their expiry date that the pharmacy is able to take depending on factors such as resources and seasonal supply problems.

Quantity to order:
- The amount to order is based on
  - stock according to the inventory when the order is made
  - safety stock
  - working stock
Order = (working stock + safety stock) - remaining stock on the day the order was made.

Inventory
- At least once a year, but if possible before every order, an inventory of the quantities actually in stock and their expiry dates should be made.
- The stock cards give a theoretical figure for the stock, but the quantities actually available should be checked product by product.
- Differences can arise through theft or errors in the record-keeping. These differences should be thoroughly investigated.
- An inventory can be made easily in a correctly arranged pharmacy.
- During the inventory, there should not be movement of stock.

PRESERVATION AND QUALITY OF THE DRUGS
- For an effective treatment, it is vital to maintain the quality of the drugs, which means that their identity, dosage and condition have to be assured.
- Storage and climatic conditions (temperature, humidity and light) may affect drug quality.
- Drugs do not lose their efficacy suddenly at the expiry date. The deterioration rate process is very slow and varies widely.
- A product may come in various forms with varying deterioration rate.

Drug Quality
To obtain good quality drugs, try to acquire them in the best possible manner by
- dealing with reliable suppliers.
- assure quality maintenance through optimum transport and storage conditions.
- Choice of a supplier should never depend exclusively upon price.

Identification
- All drugs should be easily identifiable, both by the medical staff and the patient (client).
- In whatever form the drug is packed (bottle, bag or box), it must bear not only the name of the product inside, but also its dose and expiry date.
Different products often look alike, or on the other hand, the same products may exist in different colours and/or form (e.g. tablets or capsules).

**Stability and Storage – Temperature**

- Temperature, air and light influence the storage of drugs
- Standard storage temperatures:
  - Deep freeze - -15 to 0°C
  - Refrigerator - 0 to +6°C
  - Cooled - +6 to +15°C
  - Room temperature - +15 to +30°C
- Temperatures during transit and transport reach 56°C to 60°C in vehicles, or on loading platforms.
- This means that very often, the original expiry dates cannot be guaranteed.
- Freezing can cause precipitation of the active ingredients in solutions or break the ampoules.

**Stability and Storage – Air**

- Drugs may also be damaged by the influence of humidity and oxygen
- Therefore all drug containers must remain closed
- Special medical packing often opaque and waterproof, offers protection against the influences of air and light.
- Avoid repackaging, until first distribution

**Stability and Storage – Light**

- Excessive light may also harm drugs
- Solutions are particularly sensitive to light
- Injectable preparations have to be kept in the dark in their original packing
- Certain types of coloured glass give the misleading impression that they protect drugs from light.
Expiry date
- Packaging should bear the expiry date and any specifications as to storage conditions.
  - Minimum period is usually between 3 and 5 years.
  - Common antibiotics, hormone preparations, vitamins and liquid drugs in general will last 3 years from the date of manufacture.
  - Other sophisticated products have only a 1 to 2 year period before they expire.
  - These specs do not apply to products that have to be stored under special conditions (refrigerated).
  - Disposable materials in sterilized packs may be used as long as the packaging remains intact.

Deterioration
- to detect any changes as soon as they occur it is essential to be well acquainted with the normal characteristics of every drug (colour, smell, solubility, appearance).
- certain processes may however occur without any detectable change in the appearance of the products.

Consequences of Deterioration
- Antibiotics that have expired, and become less active, may encourage resistant strains.
- Changes may result in the formation of dangerous substances and increase in toxicity e.g tetracycline would be dangerous to use when it has become brownish and viscous even before the expiry date is reached.
- Drugs which lose their effectiveness may cause increased allergic reactions e.g penicillin and cephalosporin.

Dealing with Deteriorated Drugs
- Any loss in effectiveness should not be compensated for by administering higher doses, since this may lead to serious risks of overdosage.
- Do not use suppository, creams or ointments that have melted because of the heat. The active substance will no longer be homogeneously mixed.
Dealing with Expired Drugs

- Because of our tropical environment and the lack of adequate infrastructure to store drugs properly, the use of expired drugs must be avoided.
- Incinerate expired drugs and bury residual materials at a great depth, far away from any well or water reservoir.
- Keep a special spot for this operation