SUMMARY

Cytotoxic drugs are those drugs which in their smallest effective doses, interfere with one or more of the specific processes involved in protein synthesis and cell division. Many of these cytotoxic agents act on cells that are in the process of rapid division whether normal as skin and hair follicles, or abnormal, as human malignancies and psoriatic epidermis, and this action may kill the cells or cause mutagenesis and carcinogenecity.

Some cytotoxic drugs can cause immunosuppression by inhibiting purine and pyrimidine synthesis, which in turn inhibit nucleic acid synthesis and protein synthesis. Lymphocytes and monocytes macrophages, the key mediators of immunity, like cells in other organ systems deprived of adequate nucleic acids or proteins and nucleoprotein, will not grow or replicate or synthesize protein, thus antibodies, monokines and lymphokines are not synthesized. However the exact interaction between immunosuppressives and cytotoxic drugs is still not known.

Inadequate therapy or repeated courses of immunosuppressives and cytotoxic agents may lead to resistance to the drug.

Cytotoxic drugs are effective in hyperproliferative diseases specially psoriasis, lamellar icthyosis, epidermolytic hyperkeratosis and pityriasis rubra pilaris. In these diseases the cells are rapidly replicating and so, selected out by their metabolic requirements, are inhibited earlier and to a more profound degree than slow replicators in other parts of the body.

The immunosuppressive action of cytotoxic agents can affect many diseases of altered immunity and inflammation as: bullous diseases like pemphigus vulgaris and bullous pemphigoid (specially treated with cyclophosphamide and azathioprine); the connective tissue diseases as systemic lupus erythematosus (specially treated by cyclophosphamide), progressive systemic sclerosis, progresive systemic vasculitis, periarteritis nodosa and leukocytoclastic angiitis. Also, T cell diseases may be considered in this category specially lymphoma as mycosis fungoides. The sezary varient is treated specially by methotrxate and early sarcoidosis is treated by cyclophosphamide and azathioprine.

Cytotoxic drugs can also be used in viral diseases as they inhibit virus replication but in the same time they also inhibit host cell replication. The use of cytotoxic agents in viral diseases should be reserved for those diseases which are life-threatening as herpes simplex in neonates (the best drug is acyclovir).

Cytotoxic drugs can be classified into:

* Antimetabolites, which compete with naturally occuring substances for specific enzymes, and they are subdivided into folic acid, purine and pyrimidine antagonists.

* Alkylating agents, which act by abnormal base pairing of guanine and thymine residues, abnormal pairing of two guanine residues and pairing of a guanine residue to a protein. They are subdivided into Nitrogen mustards, triazene derivatives and nitrosoureas, ethylenimine derivatives and alkylsulfonates.

* Alkaloids of colchicum autumnale, which act by binding specifically with the protein tubulin of cellular microtubules with subsequent arrest of mitosis, inhibition of granulocyte migration thus breaking the inflammatory reaction and inhibition of release of histamine and insulin. These alkaloids include colchicine, demecolcine and colcemid.

* Podophyllin, which also act by binding with protein tubulin.

* Synthetic drugs; including hydroxyurea and procarbazine.

Hydroxyurea acts by inhibiting DNA synthesis through its action on the target enzyme ribonucleoside diphosphate reductase.

* Antibiotics, including dactinomycin and bleomycin which causes fragmentation of DNA chain.

There are many cytotoxic drugs used topically in addition to their other routes of administration. These drugs include: methotrexate, 5-fluorouracil, mustine, carmustine, lomustine, colchicine, demecolcine, colcemid, podophyllin, hydroxyurea and bleomycin.

Cytotoxic drugs have many adverse reactions such as: bone marrow suppression, induction of lymphoma and leukemia, infection, hemorrhagic cystitis, bladder carcinoma, cardiomyopathy, hepatic cirrhosis, pulmonary fibrosis, gonadal dysfunction, bone necrosis and dermatitis. These side effects can be minimized when proper choosing and monitoring of the patient are done by many steps including complete physical examination of the patient both before and during treatment and laboratory assessment as liver and kidney function, urinalysis, and peripheral blood and platelet count.

At last it is important to reiterate that most severe adverse reactions to cytotoxic drugs occur in patients who are improperly or inadequately monitored, and in order to properly monitor patients who are receiving special cytotoxic agents, the therapist must be aware of at least the most common and severe adverse effects.