TREATMENT OF SIDE-EFFECTS OF CHEMOTHERAPY

The purpose of treating cancer cells with chemotherapy is to prevent them from dividing, invading and metastasizing. Most chemotherapeutic agents exert their effect on cell multiplication: obviously, since multiplication is a characteristic of many normal cells, chemotherapeutic agents will inevitably affect also normal cells and especially those with a rapid rate of multiplication and turnover such as those of the hair, intestinal mucosa, blood and bone marrow. This explains the common toxic effect of chemotherapy on the hair (hair loss), the intestines (vomiting and diarrhoea), the blood (affecting blood counts) and bone marrow (affecting the immune system).

Inhibition of cell multiplication can take place at several levels within the cell:

- Macromolecular synthesis and function
- Cytoplasmic organization
- Cell membrane synthesis function
- Environment of cancer cell growth

Most agents have their primary effect on either macromolecular synthesis or function. They interfere with the synthesis of DNA, RNA or proteins or with the appropriate functioning of the molecule. When interference with macromolecular synthesis or function of the neoplastic cells is sufficiently great, a proportion of the cells die. Because only a proportion of the cells die as a result of a given treatment, repeated doses of chemotherapy must be used to continue to reduce their number.

Neoplastic cell death may not take place at the time of exposure to the chemotherapeutic agent. Often the cell must undergo several divisions before the lethal event that took place earlier results in death of the cell. This means that the effect of chemotherapy may last for several weeks after the end of the treatment: likewise with its toxic effects on normal cells. This has important implication for our protocols with *Chemo-Support* as it means that we need to continue tonifying Qi and Blood for some time after the end of the treatment (see below).

TOXICITY

The toxicity of chemotherapeutic agents (and also of other drugs) is not a fixed entity but it varies according to several factors:

- Toxicity of specific agent
- Dose
- Schedule of administration
- Route of administration
- Predisposing factors of the patient which may be known or unknown before the start of the treatment
- Sex (women tend to develop toxicity at a lower dose than men)

COMMON TOXICITIES

Some toxicities are relatively common among chemotherapeutic agents. Common acute toxicities include:

- Myelo-suppression with leukopenia, thrombocytopenia and anaemia
- Nausea and vomiting
- Mucous membrane ulceration
- Alopecia

Apart from nausea and vomiting, these toxicities occur because of the cytotoxic effect of chemotherapy on rapidly-dividing normal cells in the bone marrow, mucous membranes and hair.

The side-effects of chemotherapy vary greatly according to the agent used. Agents may be broadly classified into four groups:

Alkylating agents damage the programs that control growth in the chromosomes of the tumour cells. Example: busulfan, carboplatin, carmustine, chlorambucil, cisplatin, cyclophosphamide, dacarbazine, doxorubicin, estramustine, ifosfamide, lomustine, mechlorethamine, melphalan, semustine, thiotepa.

Antimetabolites interfere with the manufacture of nucleotides, the substances that make up the DNA. Example: azacitidine, capecitabin, cladribine, floxuridine, fludarabine, 5-fluorouracil, gemcitabine, mercaptopurine, methotrexate, pentostatin, raltitrexed, thioguanine, trimetrexate.

Natural products interfere with cell structure and cell division. Example: asparaginase, bleomycin, dactinomycin, daunorubicin, docetaxel, doxorubicin, epirubicin, etoposide, idarubicin, irinotecan, plicamycin, mitomycin, mitoxantrone, taxol, teniposide, topotecan, vincristine, vinblastine.

Hormones block the effect of oestrogen by acting on the oestrogen-receptors. Example: aminoglutethimide, anastrozole, bicalutamide, dexamethasone, diethylstilbestrol, fluoxymesterone, flutamide, goserelin, leuprolide, letrezole, nilutamide, raloxifen, tamoxifen, torenufen.

Miscellaneous agents: altretamine, amifostine, amsacrine, dexrazoxane, hydroxyurea, mitotane, pamidronate, porfimer, procarbazine.

Biologic agents
Monoclonal antibodies: rituximab, trastuzumab.
Interferons: interferon-á2a and interferon-á2b.
Interleukins: aldesleukin, oprelvekin.
Myeloid- and erythroid-stimulating factors: erythropoietin, filgrastim, sargramostim.

SHORT-TERM SIDE-EFFECTS OF CYTOTOXIC DRUGS

Short-term side-effects of cytotoxic drugs include:

Loss of appetite
Nausea
Vomiting
Stomatitis
Malaise
Flu-like feeling, fever
Cystitis
Haematuria
Constipation
Diarrhoea

LONG-TERM SIDE-EFFECTS OF CYTOTOXIC DRUGS

Long-term side-effects of cytotoxic drugs include:

Cardiac toxicity (usually from high doses of doxorubicin or daunorubicin). Doxorubicin is widely used for breast carcinoma. If radiation is administered to the chest, the cardiac toxicity (in the form of congestive cardiac failure) may occur at lower doses. This particular long-term side-effect may occur even several years after the administration of chemotherapy.

Pulmonary toxicity (pulmonary fibrosis) is associated with high doses of bleomycin but also with alkylating agents and methotrexate.

Haematologic impairment. Alkylating agents may cause cytopenia.

Immunologic impairment and myelo-suppression. Fludarabine, cladribine and pentostatin cause profound suppression of CD4 and CD8 lymphocytes and render patients treated susceptible to opportunistic infections. There may be a fall in white blood cells and platelets counts.

Skin reactions (rash, inflammation, pigmentation, photosensitivity)

Liver toxicity.

Nephrotoxicity. This is typically caused by cisplatin, oxaliplatin, methotrexate and nitrosoureas). This toxicity may be acute or chronic and in severe cases it may require haemodialysis.

Neurotoxicity (peripheral neuropathy) is typically caused by vinca alkaloids, cisplatin, oxaliplatin, epipodophyllotoxins and paclitaxel.

CNS toxicity (lethargy, fatigue, depression, headaches, poor memory and concentration)

Premature menopause may occur in women who have received certain chemotherapeutic agents such as alkylating agents or procarbazine.

SIDE-EFFECTS OF INDIVIDUAL CYTOTOXIC DRUGS

Adriamycin
Heart muscle damage, haematuria, hair loss, nausea, vomiting, mouth ulcers.

Anthracyclines
Cardiomyopathy.

Asparaginase
Anaphylaxis (allergic reaction), fever, malaise.

Bleomycin (or Blenoxane)
Alopecia, stomatitis, fever, skin reactions, nail ridging, pulmonary toxicity.

Carboplatin (or Paraplatin)
Nausea, vomiting, bone-marrow suppression, nephrotoxicity, liver function abnormalities, diarrhoea.

Chlorambucil
Myelo-suppression, amenorrhoea, azoospermia, CNS effects at high doses.

Cisplatin
Nausea, vomiting, diarrhoea, bone-marrow suppression, renal toxicity, neurotoxicity, ototoxicity, severe electrolyte abnormalities (hyponatremia, hypomagnesemia, hypocalcemia, hypokalemia), peripheral neuropathy.

Cladribine
May cause profound suppression of CD4 and CD8 lymphocytes, nausea, skin rash, fever, headache, myalgia, arthralgia.

Cyclophosphamide
Bone-marrow suppression, hair loss, nausea, vomiting, cystitis, haematuria.

Dacarbazine
Severe nausea and vomiting, flu-like feeling, malaise, diarrhoea, bone-marrow suppression.

Daunorubicin
Myelo-suppression, cardiac toxicity, nausea, vomiting, alopecia.

Doxorubicin
Nausea, vomiting, stomatitis, hair loss, bone-marrow suppression.

Epipodophyllotoxins
Neuro-toxicity (peripheral neuropathy).

Etoposide
Nausea, vomiting, hair loss, bone-marrow suppression.

Fludarabine
May cause profound suppression of CD4 and CD8 lymphocytes, nausea, vomiting.

5-Fluorouracil
Diarrhoea, mild nausea, stomatitis, bone-marrow suppression, painful, erythematous desquamation and fissures of palms and soles.

Ifosfamide
Bone-marrow suppression, nausea, vomiting, cystitis, renal toxicity.

Melphalan
Renal toxicity, nausea, vomiting, diarrhoea, hair loss, stomatitis, bone-marrow suppression, depression.