Appendix 2
The Basics of Western Pharmaceuticals

Those who seek your medical care are likely to be taking Western drugs which have distinct effects on their physical condition and vital signs, and an important aspect of your careful medical evaluation, as referred to in chapter one, is to sort through what medications they are taking. The following brief review is included to help you recognize types and classes of such medications, and to understand their effects. For more detailed information we strongly recommend you refer to a more detailed pharmacology text, such as Dr. Greg Sperber's excellent new book, *Integrated Pharmacology: Combining Modern Pharmacology with Chinese Medicine* (Blue Poppy Press, 2007).

Nervous System Drugs

Antidepressants

Major depression is associated with chemical imbalances in the brain, and is characterized by anhedonia: the loss of the ability to enjoy life or find any pleasure or comfort in it. There are often feelings of intense sadness, a strong sense of worthlessness, loss of sex drive, either insomnia or hypersomnia, and often there are thoughts of death or suicide. There are three classes of effective medications:

- **tricyclic antidepressants** such as Elavil®, Tofranil®, Sinequan® block the re-uptake of monoamine neurotransmitters (dopamine, norepinephrine, epinephrine, serotonin), thus increasing their availability at brain receptor sites. These neurotransmitters enhance alertness, facilitate coping skills, and generally improve mood.

- **Monoamine oxidase inhibitors** (MAO inhibitors) such as Nardil®, Marplan® block the breakdown of monoamine neurotransmitters, which are continuously being chemically re-cycled. This increases their concentration in the brain.

- **Selective serotonin reuptake inhibitors** (SSRI's) such as Prozac®, Zoloft®, Paxil®, Effexor®, Wellbutrin® inhibit the reuptake of serotonin,

and often norepinephrine as well, increasing the concentration of these neurotransmitters in the brain.

Side effects are frequent with these drugs. The tricyclic antidepressants have anticholinergic effects on the body which decrease parasympathetic function resulting in a dry mouth and throat, pupil dilation with possible blurred vision, tachycardia, trouble voiding, and constipation. Other side effects of these drugs or the MAO inhibitors include weight gain, impotence, postural hypotension, agitation, uncontrollable bursts of temper, or even hallucinations or seizures. The SSRI's such as Prozac can cause headaches, nausea, diarrhea, nervousness, skin rashes, or insomnia. About 15% of those started on Prozac must be taken off the drug because of side effects such as these, but the other 85% stay on it.

Drugs for Attention Deficit Disorder (ADD)

ADD, which diagnosis now includes ADHD (with more of a hyperactivity component) is characterized by restlessness, easy distractibility, short attention span and compulsivity. Amphetamines or similar-acting drugs are mild CNS stimulants that reduce or even eliminate symptoms in almost 90% of children who take them reliably and appropriately. Dextro-amphetamine (Dexadrine®), methyphenidate (Ritalin®) and the newer, longer-acting drug Pemoline (Cylert®) have the paradoxical effect of stimulating the child's brain in ways that cause the child to focus himself and pay attention better. These drugs are combined with family counseling and psychotherapy for best results.

The most common side effect is CNS overstimulation, with insomnia, dizziness, agitation, loss of appetite. Hypertension can sometimes occur, or even cardiac arrhythmias. Patients need to be carefully monitored and changed to another drug or have the drug withdrawn without replacement if these occur.

Drugs for Psychosis

The actions of these drugs are complicated but they work to block some of the serotonin receptors in the brain that seem to be over-stimulated in psychosis. Examples of successful drugs are Chlorpromazine (Thorazine®), Triflupromazine (Vesprin®), and Thirodizine (Mellaril®).

Because these drugs block so many of the serotonin receptors they may induce Parkinson-like symptoms, or acute dystonia with face, neck, and back spasms. Trials of many different drugs are undertaken to find one that works in a given patient, often with dramatic beneficial effects.

Drugs for Parkinson's Disease

Drugs that have the opposite effects of those used for psychosis are used in this common neurological disease which presents with a resting tremor of the hands (and feet in many cases), very slow small movements of the body (bradykinesia), cramped handwriting that is very small (micrographia), postural instability, a stooped posture, and a frozen stare. Neurologists use drugs in this condition that increase neurotransmission rather than block it, as with psychosis.

Many drugs are used, but the foundational pillar is levodopa, which is usually combined with a carboxylase inhibitor known as carbidopa (levodopa alone is inactived too rapidly in the peripheral tissues before it enters the brain). Another potent drug is amantadine (Symmetryl®) which stimulates the release of dopamine from the nerve terminals where it is needed.
Many other drugs are also utilized, as side effects from the main drugs tend to occur in many patients over time (nausea, vomiting, cardiac arrhythmias, jerky involuntary movements, nightmares).

Drugs for Excessive Anxiety and for Sedation

The two major classes of drugs used for these clinical situations are the benzodiazepines and the barbiturates. They are among the most widely used drugs in the U.S. as well as in many other countries (modern life is very stressful!). Here is some information about these two types of drugs:

Benzodiazepines: enhance GABA secretion in the brain, thus causing sedative effects and skeletal muscle relaxation. These drugs may also inhibit neuronal activity by other poorly-understood mechanisms. They are used to treat anxiety states, nervous tension, agitation, delirium tremens during alcohol withdrawal, and as anticonvulsants.

The most widely known and utilized is diazepam (Valium®), one of the most popular drugs of the last 40 years in America and other countries. Valium is the most rapidly absorbed of all these drugs and has a prolonged length of active time in the body. Dalmane®, Librium®, Tranxene®, and Klonopin® are also widely used long-acting drugs of this class. Shorter acting benzodiazepines include Versed®, Xanax®, Ativan®, Serax®, and Restoril®.

Barbiturates: facilitate the retention of GABA and chloride, causing sedation, a sense of euphoria, and hypnosis. These drugs are more directly sedating than the benzodiazepines, and are therefore used as sleeping medications, a supplement to general anesthetics, and for control of seizures.

Barbiturates have been widely used for much longer than the benzidiazepines, and include such famed standbys as barbital, phenobarbital, and mephobarbitol (popular since the 1930's). These three drugs are long-acting barbiturates. Well-known short-acting barbiturates include secobarbital (Seconal®, a popular sleeping pill in the 1960's and 1970's), amobarbital (Sodium Amytal®) and pentobarbital (Sodium Pentothal®, the so-called truth serum featured in many classic movies. Many depressed individuals have attempted or succeeded in committing suicide taking a bottleful of these drugs. Ultra-short acting thiopental is used as an anesthetic agent.

Side effects of both classes of drugs are similar: drowsiness, dysarthria (trouble speaking clearly), ataxia, dermatitis, and a curious paradoxical overstimulation with strange behavior due to the loss of inhibition that we normally have (similar to the effects of alcohol in this regard).

Anticonvulsants

Seizures result when there is intense hyperactivity of the brain with many uncontrollable neuronal impulses that are firing at the same time. Drugs that calm or sedate the brain are effective in treating seizures, and many of them are the same drugs used in anxiety syndromes. Examples are phenobarbital, diazepam (Valium), and lorazepam (Ativan). Other specific anti-seizure drugs include the most widely-known of all, phenytoin (Dilantin®), along with carbamazepine (Tegretol), and valproic acid (Depakote).

Whereas the anti-anxiety drugs work by enhancing the effects of GABA, the brain's natural sedative, Dilantin, Tegretol and Depakote reduce the transport across cell membranes of sodium, potassium, and calcium, which are important in the transmission on nerve impulses. There are many other drugs which are also used for seizures that are less well-known.

Anti-anxiety drugs, when used for seizures, have side effects that we've mentioned, including drowsiness, ataxia, dysarthria, or other signs of CNS depression. Dilantin has a curious side effect which is quite common: gingival hyperplasia (buildup of excessive gum tissue in the mouth), as well as nystagmus (twitching of the eyeballs).

More serious side effects can occur with all three of these drugs, including severe liver toxicity or bone marrow suppression. Blood counts and liver function tests must be followed closely with patients who are on these drugs because

of the possibility of aplastic anemia, as well as fatal liver toxic reactions, especially in children.

Drugs for Pain Control

Morphine and morphine-like drugs bind with the opioid receptors and block pain perception.

Morphine has many side effects, including respiratory depression, constipation which can be rather severe, and a curious spasm of the bile ducts which renders it unsafe to use in patients who have gallbladder disease or biliary colic from gallstones. Nausea and vomiting are not uncommon, especially with initial doses, which may later on go away with repeated use.

Because of these side effects of morphine, pharmacologists developed other opoid narcotics which are also powerful pain-killers, although not quite as strong as morphine. These include levophanol (Levo-dromoran®), oxymorphone (Numorphone®), oxycodone (Oxycontin®), hydrocodone, hydromorphone (Dilaudid®), and the popular drug meperidine (Demerol®). Methadone is also a very effective narcotic analgesic, and is less addicting than some of the other narcotics. It is used in drug addiction clinics to help addicts withdraw from narcotics. Another powerful narcotic that has become very popular as a preoperative medication is fentanyl (Sublimaze®). It has the benefit of being less likely than morphine to cause respiratory depression.

Side effects of these other narcotic agents are similar to morphine but less pronounced. All these drugs are addictive when taken for prolonged periods of time and all lead to tolerance, requiring more of the drug for the same effect.

Weaker Narcotics

There is also a group of weaker narcotic analgesics, the classic of which is codeine. A small percentage of codeine is converted to morphine when it is ingested by mouth (about 10%). Its pain-killer activity is due to the morphine. There are also other similar drugs, such as Talwin®, Darvon®, and Nubain® which are milder in their analgesia than the strong narcotics and have the same side effects to a similar lesser degree.

Combinations of weak narcotics and NSAIDs (non-steroidal anti-inflammatory drugs) are among the most popular drugs. All require prescriptions and are used for recovery from surgery, headaches, dental pain, muscular aches and pains, where the "big guns" are not needed, with all their addiction potential.

Here is a good list:

- Tylenol with codeine No.3: 30 mg of codeine and 325 mg of Tylenol
- Tylenol with codeine No. 4: 60 mg of codeine and 300 mg of Tylenol
- Vicodin: 5 mg hydrocodone and 650 my of Tylenol
- Percocet: 5 mg oxycodone and 325 mg of Tylenol
- Percodan: 4.5 mg of oxycodone, 0.38 mg oxycodone, 325 mg aspirin
- Fiorinal with codeine No. 3: 30 mg of codeine, 325 mg of Tylenol, 40 mg of caffeine, and 50 mg butalbital (used for migraine headaches)

Narcotic Antagonists

Two drugs are widely used in hospital and emergency rooms to combat narcotic overdose: naloxone (Narcan®) and naltrexone (ReVia®). Both block opioid receptors and reverse the effects of narcotics. They are commonly used in cases of narcotic overdose in the hospital with respiratory depression, or with drug addiction overdose. These drugs, if used repeatedly, have the side effects of narcotic withdrawal: extreme restlessness, agitation, fever, muscle contractions, diarrhea, nausea and vomiting.

Drugs to Raise Blood Pressure

In cases of neurogenic, anaphylactic or toxic shock we want to raise the blood pressure and increase the perfusion of vital organs. We can do this by using drugs that cause vasoconstriction, those that stimulate the heart to beat stronger, or both. Sympathomimetic agents, most of them catecholamines, stimulate the sympathetic nervous system by attaching to alpha 1 and beta 1 receptors. These include epinephrine itself (adrenaline) and norepinephrine (Levophed®).

Drugs that preferentially stimulate beta 1 receptors promote a stronger and more rapid heart rate, without causing vascoconstriction. These include isoproterenol (Isuprel®), dobutamine (Dobutrex®) and dopamine (Intropin®).
A large number of non-catecholamine drugs are also sympathomimetic, including phenylephrine (Neo-Synephrine®) and methoxamine (Vasoxyl®). Both of these cause intense vasoconstriction and raise blood pressure by stimulating alpha receptors. They are also used in smaller concentrations in cold remedies to shrink swollen and congested mucus membranes in the nose and throat.

Side effects of all the sympathomimetic drugs result from overstimulation:

hypertension, convulsions, strokes, confusion, fever, tremors, and restlessness.

Drugs that cause Bronchodilation

Some drugs stimulate beta 2 receptors which preferentially affect the lung bronchioles, relaxing them and counteracting the bronchospasm of asthma. These include Alupent®, Ventolin®, Brethine®, and Maxair® (their generic names are not well-known). These medications can be aerosolized in an inhaler, with dose-controlled puffs.

Drugs used for Treating High Blood Pressure

Some of these agents operate by blocking alpha 1 receptors, such as Dibenzyline and Minipress. Others work by stimulating alpha 2 receptors, such as Catapres and Aldomet. In both cases, blood pressure is lowered. Other agents block norepinephrine release form the nerve endings, such as guanethidine ((Ismelin®) and reserpine. These also lower blood pressure.

Drugs that work as beta blockers also lower blood pressure by relaxing the heart and decreasing its force of contraction. Perhaps the best known of these is propranolol (Inderal®), a potent beta 1 and beta 2 blocker. It is contraindicated in patients with asthma because the beta 2 blockage causes bronchoconstriction, especially in asthmatic patients. Other agents that are more specific beta 1 blockers are used widely to rest an overworked heart (where it is not failing but simply needs more rest). Potent drugs in this category include Lopressor, Tenormin, and Zebeta, all in wide usage today. In cases of hypertension, angina pectoris, or actual myocardial infarction these drugs can be very helpful, if the patient does not have a tendency to go into heart failure. These decisions are best made by a cardiologist.

Drugs that Stimulate Acetylcholine Secretion

Acetylcholine itself can be administered as a drug but it is so powerful that it tends to over-stimulate the entire parasympathetic nervous system, slowing the heart, constricting the airways, causing over-stimulation of GI secretions, an erection of the penis, and urinary incontinence with relaxation of the urethral sphincter and contraction of the bladder. Weak doses are used in eye surgery to cause a powerful constriction of the pupils when performing cataract surgery or for treating glaucoma.

More gentle effects of parasympathetic stimulation occur with the so-called

acetyl cholinesterase inhibitors. These drugs block cholinesterase, which normally deactivates acetylcholine, thus increasing its concentration in the nerve endings and in the synapses. These drugs have fewer side effects and are used in treating such conditions as myasthenia gravis, paralytic ileus following surgery (to wake up the gut after general anesthesia puts it to sleep!), and to help treat patients who have overflow incontinence because of poor bladder contraction. These drugs include neostigmine (Prostigmine®), edrophonium (Tensilon®), and pyridostigmine (Mestinon®).

Cardiovascular Drugs

Diuretics

The first line of defense in treating hypertension is not a nervous system drug. Our first approach is lifestyle modifications, including stress reduction, weight control, exercise, and emphasis on nurturing relationships. If drugs are needed because of a high risk situation (as with a diabetic patient) the first class of drugs we use is the diuretics. These reduce blood pressure by decreasing blood volume through increased urine production. All these diuretics enhance water and sodium secretion. Their effect on other ions such as potassium depends on the drug.

The leading diuretic is chlorthiazide (Diuril®), popular for the past 50 years and still widely used. It inhibits sodium, chloride and potassium reabsorption in the distal tubules of the kidney nephrons, bringing out water along with the excretion of these ions in the urine. Gentle in its action, it is an ideal staring drug for hypertension or edema from heart failure. The main side effect is low serum potassium and calcium, and these must be closely monitored by blood tests, with supplemental potassium and calcium if not enough is taken in with the food (vegetables, bananas, milk products).

Potassium sparing diuretics are now popular, including spironolactone (Aldactone) and Dyrenium (turns urine blue!). More powerful diuretics are used in cases of severe pulmonary edema or fluid retention for other reasons (sepatientic shock, for example). These include furosemide (Lasix®), bumetanide (Bumex®) and ethnacrinic acid. These are sometimes used in hypertensive crises along with alpha blocker agents.

Alpha and Beta Blockers

These agents are widely used to treat hypertension (alpha blockers) and heart disease (beta blockers).

ACE Inhibitors

These highly popular drugs inhibit angiotensin converting enzyme (ACE) in the lung which normally converts angiotensin I to the potent vasoconstrictor angiotensin II. The most commonly used agents include captopril (Capotin®), lisiinopril (Prinivil®) and enalapril (Vasotec®). Newer drugs in this class actually block the actions of angiotensin II at the vascular receptors. These angiontesin II antagonists include losartan (Cozaar®), and valsartin (Diavan®). There are very effective in controlling high blood pressure. Side effects are hypotension and dizziness.

Direct Vasodilators

Diazoxide (Hyperstat®) is a direct acting vasodilator that is very quick and powerful in reducing blood pressure in a hypertensive crisis. Given IV, it blocks smooth muscle constriction by decreasing calcium in ways that are not completely understood. It is used for short-term control of severe hypertension in a hospital setting, preferably in the ICU. Side effects include hypotension and shock as well as hypoglycemia which may be difficult to reverse. This is an effective but dangerous drug, used in conditions where close monitoring is available.

Calcium Channel Blockers

These drugs also have a role in treating hypertension, but their main usage is in treating heart disease. They block the release of calcium from the so-called channels (where it resides when it is inactive) which is an all important step in smooth and cardiac muscle contraction. When these agents are administered to patients the heart becomes more relaxed, is less irritable, and is less prone to angina in patients who have coronary artery insufficiency.

These drugs are also very useful in patients (often young men and women) who suffer from episodes of PSVT (paroxysmal supraventricular tachycardia). These episodes feel like a flip-flopping heart to the college student experiencing them and they often last for a minute or two, then resolve. The drug of choice for treating PSVT, or PAT, as it is sometimes called, is a calcium channel blocker known as verapamil (Isopten®). Other calcium channel blockers that are widely used include diltiazem (Cardizem®) and nifedipine (Procardia®). There are also many others in use. In many cases a calcium channel blocker may be used in conjunction with a beta blocker. Cardiologists can individualize such treatment.

Anti-angina Coronary Artery Dilators

Nitrogylcerin remains the most commonly used agent for angina; usually placed under the tongue for rapid onset of action. It reaches it peak effect in 1-2 minutes and lasts for about 30 minutes. Isorbide dinitrate (Isordi®) is longer acting and is used to prevent attacks. Because it takes 5 minutes to become effective it is not used for acute attacks. Side effects are few, but include occasional hypotension in a few patients, with the possibility of rebound tachycardia because of falling blood pressure, which can make the angina worse.

Drugs for Treating Heart Failure

Digitalis is the standard drug for heart failure, and it comes in various preparations in terms of onset of action and length of activity. Digoxin (Lanoxin®) is a true miracle drug for the heart. It increases the force of contraction of myocardial muscle cells by its effects on calcium and sodium, causing increased cardiac output in a weakened heart that is failing, resulting in decreasing heart size as it becomes more efficient, decreasing edema with decreased venous return. It thus increases renal perfusion and helps the kidneys get rid of extra fluid that has been building up in the body. A loading dose of digitalis is given followed by a smaller maintenance dose. When needed, there is nothing else quite like digitalis.

Side effects are common with this potent drug, including what is known as digitalis intoxication when too much is on board, with bradycardia, and an irritable heart muscle that is prone to arrhythmias. Nausea and vomiting are also common with overdose, which often helps the patient keep the dose in check!

Beta blockers and ACE inhibitors have also been found to be helpful in treating patients with heart failure. Some patients have a variety of heart medications they are taking, carefully followed by a cardiologist or a competent internist.

Drugs for Cardiac Arrhythmias

Calcium channel blockers such as verapamil are used in treating many cardiac arrhythmias. This drug was already mentioned as a treatment for PSVT and is also used in treating atrial flutter and multifocal atrial tachycardia, and atrial fibrillation, as well as other less common arrhythmias. Beta blockers such as propanolol are also used, as are other specific agents for arrhythmias such as Quinidine and Procaine Amide. Side effects are not uncommon, including nausea and vomiting and diarrhea. Procaine Amide can cause a lupus like syndrome in some individuals, which resolves when the drug is discontinued.

Lipid Lowering Agents

The pharmaceutical industry has focused attention on agents which have been found to lower serum cholesterol and have specific effects in lowering the more dangerous fractions, LDL (low density lipoprotein) and VLDL (very low density lipoprotein) which are related to arteriosclerotic plaque formation when in high concentration. HDL (high density lipoprotein) is actually protective and helps remove cholesterol from such plaques. Agents which lower cholesterol and other lipids such as triglycerides include cholestryramine (Questran®), which acts in the gut to form insoluable complexes with bile products, thus decreasing the absorption of chemical precursers to the formation of cholesterol.

Statin drugs inhibit the formation of cholesterol in the liver and thus lower it in the bloodstream. These are tremendously popular agents in America today, and include lovastatin (Mevacor®), atorvastatin (Lipitor®), rosuvastatin (Crestor®), and many others. Gemfibrozil (Lopid®) is used to lower high levels of triglycerides by increasing lipoprotein lipase activity.

Recent research has questioned the use of these drugs, which have many side effects, such as muscle cell breakdown, increased incidence of Alzheimer's disease and other neurological dysfunctions due to lipid breakdown in nerve cells, and many others. Research has shown these lipid lowering drugs reduce mortality in high risk patients, but not in those who take them simply as a preventative but who are not at high risk. It may be that the main causes of atherosclerotic plaque disease in coronary and cerebral arteries are chronic inflammation and oxidative effects associated with obesity, improper diet, and lack of exercise.

Anticoagulants, Thrombolytics, and Antiplatelet Agents

Anticoagulants are used to inhibit blood coagulation in cases where blood clots have formed or are likely to form. Heparin is the most powerful, inhibiting the clotting cascade at several levels and inactivating thrombin. It is used IV or subcutaneously in cases where there is a significant risk of deep vein thrombosis and possible pulmonary embolism, such as during open heart surgery, hemodialysis, or during any operation where the risks of intraoperative or postoperative blood clots are considerable (especially orthopedic surgery).

Heparin is also used to treat deep vein thrombosis and pulmonary embolism, preventing the formation of any new clots and allowing the body's own fibrinolytic mechanisms to break down clots that have already formed.

Coumadin (also known as warfarin) is a less powerful anticoagulant but is still effective in preventing blood clots and it can be taken by mouth. Usually following a deep venous thrombosis the patient is admitted to the hospital for a week of heparin treatment IV, followed by six months to a year of p.o. coumadin afterward to prevent new clots from forming in damaged or inflamed veins. Coumadin antagonizes vitamin K activity, and thus prevents the action of several clotting factors which depend on vitamin K (II, VII, IX, and X).

Patients are also placed on coumadin who are in atrial fibrillation and cannot be converted to a regular sinus rhythm, to prevent clots from forming on the walls of the atrium that is not beating effectively that might flow out of the heart and occlude a cerebral vessel, causing a stroke. I know personally of sad cases of individuals who were in atrial fibrillation and experienced GI upset from coumadin and simply stopped taking it, with disastrous results (death from a stroke).

Thrombolytic agents activate plasminogen, which dissolves blood clots. They are thus the most powerful agents against blood clots, but must be used when the clots are freshly formed or they are not effective. The most popular is recombinant tissue plasminogen activator, rtPA (Alteplase®). It has been proven very effective in reducing mortality and morbidity after thrombotic strokes, if used within the first three hours. Other thrombolytic agents such as streptokinase and urokinase are available but are not as effective as rtPA.

Antiplatelet agents prevent platelet coagulation, which is in important part of clot formation. The classic and most popular is aspirin; still used in myocardial infarctions to prevent propagation of the clot in the coronary artery to other branches. Prophylactic use of a small dose of aspirin every day reduces the risk of a heart attack or a stroke, and everyone should carefully consider taking aspirin in this manner. Ibuprofen is also used as an antiplatelet agent. Both of these drugs have the risk of GI ulceration and hemorrhage, especially ibuprofen. Other antiplatelet agents are also dispensed by physicians, such as Plavix and Persantine.

Drugs used in Treating COPD and Asthma

Bronchodilators are very useful in these conditions, such as albuterol (Ventolin®), metaproterenol (Alupent®), and terbutaline (Brethaire®), all of which are beta 2 adrenergic stimulants. Muscarinic antagonists (see above) such as ipratropium (Atrovent®) are also very useful and do not have the side effects of the sympathomimetic agents listed above, which stimulate the heart and can cause tachycardia. Theophylline and aminophylline are caffeine-like xanthine drugs which also cause bronchodilation and are often used in COPD.

Corticosteroids are powerful anti-inflammatory agents that are also very useful in treating COPD as well as some cases of severe asthma, as they reduce the swelling in the bronchial passages. The most popular are dexamethasone (Decadron®) and triamcinolone (Azmacort®), but many others are also used.

Inflammatory cell stabilizers are useful in bronchospasm lung conditions, which prevent the release of inflammatory-provoking mediators such as histamine from the mast cells and eosinophils. Cromolyn is the most popular. It does not act swiftly and thus cannot be used during an asthma attack.

Leukotrine receptor antagonists are becoming among the most popular drugs with asthmatic patients. They inhibit the release of leukotrines from white cells (other than histamine) which also cause bronchospasm in allergic asthma. The most popular are Singulair and Accolate. Like cromolyn, they are not used during an attack but are taken to prevent attack from taking place. These drugs have vastly improved the lives of many asthmatics.

Mucolytic agents are helpful in breaking up and reducing the viscosity of mucus secretions and liquifying them, helpful in many lung conditions. Mucomyst® is an example of such an agent. Many others are also available.

Drugs for Stomach and Other Digestive Disorders

The antisecretory agents that are used are proton pump inhibitors, such as omeprazole (Prilosec®), or esomperasole (Nexium®), or H2 histamine receptor antagonists, such as ranitidine (Zantac®). These drugs reduce gastric acid as a result of complex pharmacological effects on protons that are important in producing acid in parietal cells, or in blocking specialized histamine receptors that play a role in HCL production This decreased acid secretion promotes healing of the ulcer or the gastritis. Bismuth is also widely used. It forms a protective

coating and has antibacterial effects of its own (it is also used as an antidiarrheal agent).

Reflux esophagitis or GERD (gastroesophageal reflux disorder) is common to modern Americans, causing heartburn that radiates from the stomach into the throat. There is usually an incompetent lower esophageal sphincter. The condition is exacerbated by obesity, smoking, and the consumption of spicy food and junk food. The above-mentioned antisecretory agents are also very helpful in treating GERD, especially when combined with lifestyle modifications and discontinuance of smoking (nicotine relaxes the GI sphincters and can make GERD worse as a result).

Antidiarrheal agents

Diarrhea (dia–through, rhea–flow) is a common experience for most humans, usually caused by toxic substances in the diet (food poisoning), drug reactions, or either viral or bacterial infections. Suspicious drugs should be stopped, of course; perhaps substituted for some other drug if such treatment is necessary. Most other cases of diarrhea are self-limiting over 1-2 days, and respond to the BRAT diet (bananas, rice, apple sauce, and tea, to calm the intestinal tract and replace lost electrolytes such as potassium and sodium).

Bacterial infectious diarrhea is more serious, presenting with fever, abdominal pain, and bloody diarrhea. Stool samples show white cells and cultures are often positive for Salmonella, Shigella, Camplylobacter, or Staphlococcus. Appropriate antibiotics are needed (often ciproflocacin or doxycycline). Guiardia diarrhea is caused by a parasite that shows up in the stool of campers. It responds to metronidazole (Flagyl®).

Laxatives

Most episodes of constipation are transient. Many are related to travel, change in activities or diet, or prolonged immobilization after surgery or accidents. More severe forms can be due to certain drug reactions (narcotics, anticholinergics). Constipation is common in the elderly. Conservative treatment is with increased fiber in the diet, and, if needed, bulk-forming agents such as Metamucil or Mitrolan, which have no side effects.

Other agents for constipation include stimulant laxatives such as bisacodyl (Dulcolax®), cascara, or senna. Chronic use of these agents can cause real dependency on them. Senna may actually damage the nerves to the colon.

Other agents include those which draw water into the colon such as milk of magnesia, or polyethylene glycol, which has the same effect. Colace® improves the penetration of water into the feces and causes increased bulk. Mineral oil lubricates the feces and helps with elimination.

Antibiotics

To understand antibiotics it is important to remember that there are different classes of bacteria. These are often differentiated by their staining qualities, which also correlate with their behavior and their sensitivity to antibiotics. Gram positive bacteria such as Staphlococcus, Stretococccus, and Pneumococcus cause soft tissue infections and pneumonia (staph also causes infections everywhere else). Gram negative bacteria such as E. coli, Pseudomonas, Aerobacter, Proteus, Salmonella, and Shigella often cause intestinal or urinary tract infections. A variety of organisms cause sexually transmitted diseases, both bacteria (Nisseria gonorrhea,Treponema (Syphilis), and Chlamydia) and viruses (Herpes, HIV, HPV and Hepatitis). Acid-fast bacteria such as Mycobacterium tuberculosum cause nodular infections in the lungs and other areas of the body. They are slow-growing and require a long time for treatment (usually a year). Prior to antibiotics tuberculosis was one of the greatest killers on earth.

Gram positive bacteria, once sensitive to penicillin, have become very resistant to it in recent years. Most skin infections respond well to oral first generation cephalosporins (there are four generations) such as cephalexin (Keflex®) and cephazolin (Ancef®). These antibiotics are a backbone of medical practice, as such infections affect all of us at one time or another. More serious gram positive infections such as pneumonia or osteomylitis respond well to IV Nafcillin and oral dicloxacillin. Intravenous Vancomycin and Rocephin are used for methacillin resistant staph infections (MRSA).

Gram negative bacteria are common in serious intestinal tract infections (such as peritonitis from a ruptured appendix) or upper urinary tract infections (pyelonephritis). For serious infections of this sort third generation cephalosporins such as ceftriaxone are used IV, and have saved many lives. Aminoglycosides such as gentamycin are also very effective. Ampicillin and gentamycin are often used together in serious infections where the doctors don't yet know what the bacteria are (bacterial endocarditis, brain abscess), then the

treatment becomes precise once cultures and sensitivities come back in 48 hours. Amoxacillin or Augmentin (amoxicillin plus clavulinic acid) are used to treat otitis media and sinus infections, which if unchecked may lead to brain abscesses, especially in diabetic patients or the elderly.

Tuberculosis responds well to isoniazid and rifampin, taken over six to twelve months, depending on the severity of the infection.

Fungal infections in the mouth or vagina respond well to various anti-fungal agents such as mycostatin or ketaconazole. More serious systemic fungal infections may require amphotericin (those who take it often call it amphoterrible because of the nausea, vomiting, dizziness, and other side effects, but they continue to take it).

Antiviral Therapy

The list of available antiviral agents which ameliorate viral infections is growing longer every year. Here are just a few of the most popular:

- **Zanamavir** (Relenza®) and oseltamivir (Tamiflu®) moderate the severity of influenza and the bird flu virus. The government has stockpiled large quantities of these agents in case there is a bird flu epidemic, as happened in 1918 with the death of at least 50 million people.
- **Amantadine** (Symmetryl®) is used to treat influenza in the elderly, and also has a beneficial effect on Parkinson's disease through different mechanisms.
- **Acyclovir** (Zovirax®), Valcyclovir (Valtrex®), and Famcyclivir (Famvir®) are extensively used to treat herpes genitalis and herpes oralis as well as shingles (also caused by a herpes virus), although they are not curative.
- **Ganciclovir** ((Cytovene®) is helpful in treating cytomegalovirus (CMV) infections which are common in AIDS patients
- **Zidovudine** (Retrovir®), Lamivudine (Epivir®), Abacavir (Ziagen®) and other nucleoside reverse transcriptase inhibitors are used to treat HIV and AIDS, in combination therapy
- **Ritonavir** (Norvir®), Nelfinavir (Viracept®), Fosamprenavir (Lexiva®) and other drugs such as these are protease inhibitors, also used in combinations to treat HIV and AIDS

- **Nevirapine** (Viramune®) Enfuvirtide (Fuzeon®) and others are so –called non-nucleoside reverse transcriptase inhibitors, also used to treat HIV and AIDS patients

Antiparasite drugs

Parasite infections are everywhere in the tropics and throughout third world countries, where sanitary conditions are such that these larger microorganisms can survive and infect humans. Malaria kills over a million people worldwide every year. Amebiasis is a scourge that kills hundreds of thousands. Other parasites also abound in these other countries and parts of the world. Some parasitic worms craw around inside the body and then attach to the intestinal tract, where they suck the blood of the victim.

Antimalarial drugs are mostly in the quinine family, including chloroquine, hydroxychloroquine, mefloquine, and primaquine. Other drugs are also utilized depending on what the local Plasmodium species is most sensitive to. Quinine itself is still used to treat resistant cases of Plasmodium falciparum where nothing else works, but it is the most toxic of the antimalarials. They all have severe side effects. Including irreversible eye damage, dizziness, and shock in some cases.

The most common parasite infections in the U.S. are Giardia, an intestinal infection, and Trichomonas vaginalis which causes vaginitis. Both are treated with metronidazole (Flagyl®). Pinworms are common in school children, and can then infect the whole family. They are treated with mebenazole, taken by mouth by the entire family if one child shows up with pinworms, which crawl out of the anus at night and lay their eggs, causing intense anal itching. Lindane (Kwell®) is used topically to treat scabies (head, body and pubic lice). Proper attention to personal hygiene and sanitation is essential to avoid these infestations, along with careful selection of potential romantic partners in the case of scabies.

Anti-inflammatory and Immunosuppressant Drugs

Autoimmune processes provoke inflammatory responses, and pharmacologists have developed many anti-inflammatory agents over the years which are very helpful in reducing inflammation. A true wonder drug in this regard is aspirin, because it has so many beneficial effects. It lowers fever, reduces inflammation,

combats pain, and helps prevent blood clots, all at the same time. It manages to do this because it blocks the enzyme cyclooxygenase. This enzyme catalyzes the formation of a group of chemicals known as prostaglandins that travel throughout the body in times of infection, for example. These prostaglandins have a role in producing fever, encouraging platelet aggregation, provoking the inflammatory response (redness, heat, swelling, and pain) and then facilitating the perception of pain, all intended to protect us and help us cope with whatever is infecting or otherwise assaulting us.

Because these protective mechanisms such as the inflammatory response are unpleasant and often undesirable, many drugs have been developed which inhibit prostaglandin formation or action. These include aspirin and many other non-steroidal anti-inflammatory drugs (NSAIDs) such as acetoaminophen (Tylenol®), ibuprofen (Motrin®, Advil®), and naproxen (Naprosyn®, Aleve). Side effects include GI upset and bleeding, especially with prolonged use or overdose. NSAIDs are among the most widely used drugs and are over-the-counter and are thus very easy to obtain. As a result, GI bleeding as a side effect of these agents takes a heavy toll of American lives each year.

New drugs such as celecoxib (Celebrex®) selectively inhibit cyclooxygenase II and have fewer GI side effects. One of these, Vioxx®, was taken off the market because of concern it might be related to an increased risk of heart attacks and strokes. Long-term safely of these new COX II inhibitors is still being studied.

Corticosteroids are even more potent anti-inflammatory agents than NSAIDs and are a mainstay of treating autoimmune disorders, although the long-term use of steroids leads to Cushing's syndrome, with diabetes, hypertension, fluid retention, osteoporosis and stomach ulcers along with many other unpleasant features. They are nonetheless miracle drugs because of their powerful beneficial effects in reducing inflammation and swelling, even saving the lives of many individuals with closed head trauma from auto accidents and falls who might otherwise die from increased swelling of the brain with herniation of the brainstem into the upper spinal column.

Drugs which suppress the activity of the immune system have been developed which are also widely used in autoimmune disorders. These include methotrexate, azathioprine (Imuran®), cyclophoasphamide (Cytoxan®), and the newer agents that block the actions of TNF, the tumor necrosis factor, such as inflixamab (Remicaid®).

Anticancer Drugs

Cancer chemotherapy has a bad name because of the miserable and dangerous side effects of these drugs which are designed to prevent cancer cells from growing and multiplying but which also have the same effect on the body's most rapidly growing healthy cells. Nausea, vomiting, GI ulceration, immune system suppression, and loss of hair (alopecia) are but a few of these complications of therapy. Some of the newer agents are more powerful with fewer of these side effects, as noted below.

Cancer fighting drugs include many types, such as alkylating agents (the first chemotherapy agents used, which bind DNA strands together so they cannot reproduce), antimetabolites (which interfere with the building blocks of DNA synthesis), agents derived from antibiotics, which also interfere with DNA and RNA synthesis by the cancer cells, and the vinca alkaloids (such as vincristine and vinblastine) that interfere with the microtubules of the cells so they cannot develop properly.

Many of these newer agents, often used in combination, have proven powerful in treating childhood cancers such as leukemia, sarcoma, and lymphomas. Some are now so effective they can result in permanent cures; something unheard of 20 years ago. Many acute leukemias, some lymphomas, and certain testicular tumors are now potentially curable with chemotherapy.

The new monoclonal antibody agents show great promise in effectively treating many cancers, such as trastuzumab (Herceptin®), as they selectively bind to antigenic receptor sites on the cell walls of tumors, where they can carry out their cytotoxic effects.

Hormonal Agents

The most common hormonal agents used in America are thyroid replacement hormones, as hypothyroidism (often from Hashimoto's disease) is so common in middle-aged and elderly individuals. The thyroid gland secretes both triiodothyronine (T3) and tetraiodothyronine (T4) although T4 predominates in the circulation and is bound to a transport protein, thryoglobulin. T3 is more powerful in its metabolic effects than T4 and both must be released from their carrier proteins before they can enter the cells as the free T3 and T4. The most common replacement drug is levothyroxine (Synthroid®) which is T4. Most of the T4 is then converted to T3 in the periphery of the body before it enters the

cells and stimulates metabolism. A T3 agent is also available, liothyronine (Cytomel®), used in those who do not respond well to Synthroid. Achieving a proper thyroid hormone balance in the body is often more difficult with Cytomel, and many patients who take it complain of tachycardia, nervousness, and tremors. A middle-of-the-road compromise is to take Armour dessicated thyroid, from pigs (it smells like pigs) which has a combination of both T3 and T4. Internists are adept at working with patients to achieve the right balance.

Insulin comes in many forms for type I diabetic patients. Insulin must be given by injection. Short-acting insulins, intermediate-acting insulins, long-acting insulins, and ultra long-acting insulin preparations are available. Glucagon is kept handy for injection by diabetics if they feel their blood sugar is falling too low after an insulin dose and they are getting shaky or sweaty (or their glucometer tells them the glucose is too low).

There are many oral agents for type II diabetics. The sulfonylurea drugs are the most commonly used, including tolbutamide (Orinase®), chlorpropamide (Diabenese®), tolazamide (Tolinase®) and the newer second-generation agents glipizide (Glucotrol®) and glyburide (Micronase®). The newer drugs require a lower dose but basically work the same way to stimulate insulin secretion from the pancreatic beta cells. Other drugs such as metformin (Glucophage®) decrease intestinal absorption of glucose and also reduce production of glucose in the liver. Additional new classes of drugs such as rosiglitazone (Avandia®) sensitize the body's cells to insulin, especially the liver and muscle cells.

Oral Contraceptives

The discovery of the birth control pill and its FDA approval in 1960 had the greatest sociological consequences by far of any drug discovery, resulting in the sexual liberation of women. The first pill was Enovid, which was just as effective as any oral contraceptive since then but had terrible side effects, especially blood clots. Far safer oral contraceptives have since been developed. Most are combinations of estrogen and progesterone that prevent ovulation because of their effects in repressing hypothalamic and pituitary hormone secretions that normally stimulate ovulation in mid-cycle. These are almost 100% effective if taken reliably, although that doesn't always happen, and, as a result, unexpected pregnancies do occur. The pills are taken for 21 days of a 28 day cycle, with placebo or iron pills taken the remaining 7 days to maintain the habit of taking one pill a day on a reliable basis.

Newer oral contraceptives may be biphasic or triphasic, meaning they start off with low doses of progestins, which are increased in mid-point in the biphasic pills, and every 7 days in the triphasic pills, to more closely mimic the natural hormonal secretion of progesterone. The estrogen concentration remains unchanged throughout the 21 days in these preparations. These newer preparations have significantly reduced the incidence of side effects, which include breast tenderness, nausea and vomiting, water retention, and weight gain. There is a small risk of blood clots, increased in those who are smokers. Women with a history of thromboembolic disease, liver disease, cancer, cerebrovacular disease or myocardial infarctions in the past should not take oral contraceptives.

Progestin- only "minipills" are available for those who cannot or should not take estrogen preparations. They have the same dose of progestin during the entire 28 day cycle, and act in some way that is not well-understood to render the endometrium unreceptive to implantation of a fertilized ovum.

Levornogestrel implants (Norplant®) contain the progestin levornogestrel which are imbedded in thin polymer strips and imbedded under the skin, often of the forearm, continuously releasing progestin and preventing pregnancy.

Drugs to Enhance Fertility

Clomiphine (Clomid®) stimulates the pituitary to release LH and FSH, thus leading to ovulation in a large majority of women who take it. The rate of multiple pregnancies is about 8% with the use of this drug, and many women who take it experience ovarian enlargement which can cause abdominal and pelvic pain. Other drugs are also in use and being carefully studied, including purified FSH and LH (obtained from the urine of postmenopausal women) although the incidence of side effects is significant, such as ovarian enlargement, with occasional bleeding into the abdomen. Women who are highly motivated to become pregnant are willing in many cases to accept the risks of taking these drugs. Fertility enhancement is a rapidly developing field of pharmacology.

DRUG - HERB INTERACTIONS

This topic is of great concern to Asian medicine practitioners. Some reports on adverse reactions in the literature are based on research and are of serious concern; others are based on case reports and the opinions of the authors of the report and may not be based on research.

While it is important to remember that actual cases of adverse events due to a drug-herb interaction are extremely few and far between, I encourage all of you to delve further into this area of concern, which is covered in great detail in Dr. Greg Sperber's excellent new book, I*ntegrated Pharmacology: Combining Modern Pharmacology with Chinese Medicine* (Blue Poppy Press, 2007).