CENTRAL NERVOUS SYSTEM AGENTS

The central nervous system *agents have the largest amount of sub-classifications in this pharmacology section. Narcotic analgesics principally act on the sigma and mu receptors in the body to decrease the patient's perception of pain. Non-narcotic agents reduce the level of prostaglandin synthesis to decrease the inflammatory response. The cholinergic agents act by either increasing or decreasing the amounts of available acetylcholine or acetylcholinesterase. Adrenergic agents affect the sympathetic nervous system by promoting or depressing the alpha and/or beta responses. Most of these adrenergic agents are site specific (e.g., Metoprolol is* $beta_1$ *specific). The CNS stimulants act by increasing the available amount of the neurotransmitter norepinephrine which will increase cellular impulse transmission. Anti-convulsants act in several ways such as either increasing* Na^+ *evacuation or preventing its entry into the cell, elevating* GABA *levels, or decreasing acetylcholine levels. Sedatives and hypnotics reduce the activity in the* thalamus *and the* cortex *(the thalamus receives sensory input from the brain). Two major actions predominate for the anti-depressants, they either increase the norepinephrine and serotonin levels in the brain or they inhibit the production of monoamine oxidase (MAO) which breaks down the neurotransmitters. Antipsychotics block the dopamine receptor sites in the brain or decrease the responsiveness of the* medulla. *Finally, anxiolytics alter the responses in the limbic center or they increase GABA levels.*

ANALGESICS

OPIOID AGONISTS

Mechanism: Binds to opioid receptor sites and depresses and/or alters the patient's pain response. Most also provide a euphoric effect.

Indication: Pain

Examples: Codeine, Fentanyl, Hydromorphone, Oxycodone, Propoxyphene, Morphine

Side effects: Orthostatic hypotension, Dizziness, Lightheadedness, Constipation

OPIOID AGONIST-ANTAGONIST

Mechanism: Binds to the opioid receptor sites while also exhibiting a mild narcotic antagonist action. Prevents further binding of the receptor site.

Indications: Pain

Examples: Buprenorphine, Butorphanol, Nalbuphine, Pentazacine

Side effects: as above

NON-OPIOID ANALGESICS

Mechanism: Three major classes, salicylates (aspirin), para-aminophenal (Tylenol), and Non-steroidal anti-inflammatory drugs (NSAIDS, e.g., Ibuprofen). All inhibit prostaglandin synthesis which may increase the body's response to pain. They exhibit an anti-pyretic effect by either peripheral vasodilation or by acting on the thermoregulatory center.

Indications: Pain, Fever

Examples: Aspirin, Acetaminophen, Ibuprofen, Ketoprofen, Naproxen sodium

Side effects: GI problems, Tinnitus, Headache, Dizziness

CHOLINERGIC AGENTS

CHOLINERGIC AGONISTS (PARASYMPATHOMIMETIC)

Mechanism: Activate the cholinergic system by either inducing parasympathetic activity or by inhibiting the release of acetylcholinesterase (the enzyme required to break down acetylcholine).

Indications: Glaucoma, Myasthenia gravis, to increase bladder and intestinal function

Examples: Cholinergic activators: Bethanechol, Pilocarpine
Acetylcholinesterase Inhibitors: Edrophonium, Neostigmine, Physostigmine

Side effects: Hypotension, Headache, Flushing, Nausea and Vomiting, Diarrhea, Bradycardia

CHOLINERGIC ANTAGONISTS

Mechanism: Inhibits the effect of acetylcholine on the muscarinic sites

Indications: Bradyarrhythmias, Extrapyramidal reactions, Parkinsonism

Examples: Atropine, Benztropine, Glycopyrrolate

Side effects: Tachycardia, Constipation, Dry mouth

ADRENERGIC AGENTS

ADRENERGIC AGONISTS

Mechanism: Stimulates the alpha and/or beta responses of the sympathetic nervous system. Alpha$_1$ causes vasoconstriction; Beta$_1$ increases the rate, force and automaticity of the heart; Beta$_2$ produces bronchodilation and vasodilatation.

Indications: Bronchospasm, Hypotension due to CHF or heart rate deficiency, Vasoconstriction

Examples: Albuterol, Dobutamine, Dopamine, Epinephrine, Isoproterenol, Norepinephrine

Side effects: Arrhythmias, Tachycardia, Angina, Nervousness, Tremors

ALPHA ADRENERGIC BLOCKING DRUGS

Mechanism: Stimulates the release of alpha$_2$ which prevents vasoconstriction

Indications: Reynaud's disease, Vascular headache, IV extravasations

Examples: Ergotamine tartrate, Phenoxybenzamine, Phentolamine

Side effects: Orthostatic hypotension, Tachycardia, Dizziness, Numbness

BETA ADRENERGIC BLOCKING DRUGS

Mechanism: Blocks or displaces the agent from the receptor sites

Indications: Hypertension, Angina, Glaucoma

Examples: Acebutolol, Atenolol, Esmolol, Labetalol, Metoprolol, Pindalol

Side effects: Arrhythmias, Bradycardia, Bronchospasm, Nausea and Vomiting

CENTRAL NERVOUS SYSTEM STIMULANTS

Mechanism: Exact mechanism is unknown. It is believed that these agents stimulate the release of norepinephrine which will lead to an increase in nerve impulse transmission from cell to cell.

Indications: Narcolepsy, Attention Deficit Disorder, Respiratory stimulation

Examples: Dextroamphetamines, Doxapram, Methylphendiate hydrochloride, Pemoline

Side effects: Nervousness, Tremors, Irritability, Hypotension, Arrhythmias

ANTI-CONVULSANTS

Mechanism: Depresses the discharge of abnormally fired neurons by a number of different mechanisms. These mechanisms range from promoting Na^+ exit from the cell, inhibiting Na^+ from entering the cell, increasing the inhibitory effect of gamma-amino butyric acid (GABA), prevention of release of glutamate and aspartate, and decreasing acetylcholine released by the nerve impulses.

Indications: Seizures

Examples: Hydantoins (ethtoin, felbamate, phenytoin)
Barbiturates (phenobarbital, mephobarbital, primidone)
Benzodiazepines (clonazepam, clorazepate, diazepam)

Side effects: Nystagmus, Drowsiness, Hypotension, Respiratory depression

SEDATIVES AND HYPNOTICS

Mechanism: Decreases the amount of neurotransmissions form the thalamus and the cortex of the brain.

Indications: Wide ranging; from sedation and insomnia to treatment of alcohol withdrawal symptoms.

Examples: Thiopental sodium, Pentobarbital, Phenobarbital, Alprazolam, Cloracepate, Diazepam, Quazepam, Chloral Hydrate

Side effects: Drowsiness and respiratory depression

ANTI-DEPRESSANTS

Mechanism: Two primary mechanisms prevail. The first, ticyclic antidepressants (TCA), is to cause an increase in the amount of norepinephrine and serotonin in the central nervous system. This is accomplished by inhibiting the reabsorption of these two substances in the presynaptic membrane. The second is a monoamine oxidase inhibitor (MAO) that prevents the central nervous system's neurotransmitters from being metabolized. After one of these two events has occurred the rest of the mechanism is unknown.

Indications: Depression

Examples: TCA & others: Amitriptyline, Clomopramine, Doxepin, Bupraprion
MAO Inhibitors: Phenelzine, Tranylcypromine

Side effects: Hypotension, Tachycardia, Blurred vision, Dry mouth, Restlessness, Insomnia, Nausea and Vomiting

ANTIPSYCHOTICS

Mechanism: The majority of agents block the post synaptic dopamine receptors which, in turn, inhibit the transmission of nerve impulses. Some others also have the effect of decreasing the cells responsiveness at the medullary chemoreceptor zone.

Indications: Psychosis, Schizophrenia, Alcoholism

Examples: Chlorpromazine, Mesoridazine, Perphenazine, Thioridazine, Droperidol, Haloperidol

Side effects: Extrapyramidal reactions, Tardive dyskinesia, Sedation, Blurred vision, Dry mouth, Heat intolerance

ANXIOLYTICS

Mechanism: A number of actions among the various agents exist, but the vast majority appear to effect some level of the limbic or subcortical areas of the brain. One other major mechanism appears to be in the potentiation of GABA, which is an inhibitory neurotransmitter.

Indications: Anxiety, Alcohol withdrawal, Partial seizure disorder

Examples: Alprazolam, Chlordiazepoxide, Hydroxyzine, Midazolam
Side effects: Drowsiness, Respiratory depression

COMMONLY TRANSPORTED CENTRAL NERVOUS SYSTEM PHARMACOLOGIC AGENTS

This section is left blank for the services medical director or training officer to review those agents which are commonly used for transport. Topics which should be covered include dosages, indications, side effects, and any transport considerations.