CHEMISTRY AND ACTION:
DRUG TERM INDEXING IN THE MEDICAL SUBJECT HEADINGS

Most of the "things" we are interested when we conduct a literature search are really quite complicated. For example, no one really want's literature on "bacterial pneumonia"; what they really want is something more specific: treatments for the disease, or how to diagnose the disease, the epidemiology of the disease, as so on.

The Medical Subject Headings (MeSH) try to address this issue by providing a list of some 80 subheadings which can be used to qualify a heading: "Pneumonia, Bacterial / *drug therapy*" or "Pneumonia, Bacterial / *diagnosis*". And so, we are already used to the complexities of MeSH.

Similarly, drug topics also pose a particular problem. For example, all of the following papers concern the same drug, aspirin, but they are all concerned with a different effect or action of the drug:

> *TI: Randomized clinical trial of the antiplatelet effects of aspirin-clopidogrel combination versus aspirin alone after lower limb angioplasty.*
>
> *TI: Aspirin is efficacious for the treatment of acute migraine.*
>
> *TI: Effects of acetylsalicylic acid on sore throat pain and other pain symptoms associated with acute upper respiratory tract infection.*
>
> *TI: A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women.*

Years ago, the MeSH tree structures included **hierarchies** for drugs that reflected their pharmacological actions. There was an "Antibiotic" hierarchy that broke down into narrower and narrower categories until eventually specific antibiotic headings were listed. So under antibiotics were headings for broad types of antibiotics: "*Aminoglycosides*", "*Antibiotics, Lactam*", etc. A heading like "*Antibiotics, Lactam*" would in turn break down into categories like "*Cephalosporins*", "*Penicillins*", etc.

The difficulty with this approach is that many drugs, such as aspirin, don't fit into single pharmacological categories. This led to the following situation: when the "*Analgesic*" heading was exploded, it would retrieve papers assigned the MeSH heading "aspirin", but often the papers assigned this heading weren't about the analgesic effects of aspirin, but about one of it's other effects (e.g. inhibition of platelet aggregation).

So all the specific drug terms were removed from any MeSH categories which were essentially describing a "pharmacologic action".

Now the only categories which list specific drugs in their hierarchies are the chemical groups to which the drugs belong.

At the same time as this change was made in the hierarchies, the following indexing practice was initiated:

> When a paper concerns use of a drug to treat a disease or when the paper concerns some other aspect of the drug when used therapeutically (administration & dosage, pharmacology, adverse effects, etc.) the subject indexer must assign:
>
> 1. The MeSH heading for the drug or the narrowest chemical heading available.
> 2. The heading or headings that describe the *pharmacologic action* of the drug.

Often the same subheadings will be applied to both headings when the aspect they describe has to do with the drug biological action (e.g. therapeutic effect, adverse effect) or it's use as a drug (e.g. administration & dosage)

TI: **Metformin therapy and diabetes in pregnancy**.

MAJOR MESH:

- Breast Feeding /
- ***Hypoglycemic Agents / therapeutic use***
- ***Metformin / therapeutic use***
- Pregnancy in Diabetics / drug therapy

MINOR MESH:

- ***Metformin / analysis***
- ***Metformin / pharmacokinetics***
- Milk, Human / chemistry
- Practice Guidelines /
- Risk Assessment /

A CAREFUL LOOK AT A SPECIFIC MESH DRUG HEADING: ASPIRIN

The MeSH scope note for *Aspirin* notes the various therapeutic or pharmacologic actions of this drug:

Scope Note:

The prototypical ***analgesic*** used in the treatment of mild to moderate pain. It has ***anti-inflammatory*** and ***antipyretic*** properties and acts as ***an inhibitor of cyclooxygenase*** which results in the inhibition of the biosynthesis of prostaglandins. Aspirin ***also inhibits platelet aggregation*** and is used in the prevention of arterial and venous thrombosis.

As with all chemicals, aspirin is included in the MeSH tree structure based on its chemical classification:

MeSH Tree Stuctures (hierarchical categories) **under which Aspirin is found:**

Chemicals and Drugs Category	Chemicals and Drugs Category	Chemicals and Drugs Category
Organic Chemicals	Organic Chemicals	Organic Chemicals
Carboxylic Acids	Carboxylic Acids	Phenols
Acids, Carbocyclic	Hydroxy Acids	**Hydroxybenzoic Acids**
Benzoic Acids	**Hydroxybenzoic Acids**	**Salicylic Acids**
Hydroxybenzoic Acids	**Salicylic Acids**	**Aspirin**
Salicylic Acids	**Aspirin**	
Aspirin		

Note that all the categories are "chemical", none pertain to the "pharmacological action" of aspirin.

Here is the complete list of pharmacological action headings from MeSH. Note that no specific drugs or chemicals are listed.

MESH PHARMACOLOGICAL ACTIONS CATEGORY

Note: there are no narrower terms for any of the headings.

Abortifacient Agents
Abortifacient Agents, Nonsteroidal
Abortifacient Agents, Steroidal
Adhesives
Adjuvants, Anesthesia
Adjuvants, Immunologic
Adjuvants, Pharmaceutic
Adrenal Cortex Hormones
Adrenergic Agents
Adrenergic Agonists
Adrenergic alpha-Agonists
Adrenergic alpha-Antagonists
Adrenergic Antagonists
Adrenergic beta-Agonists
Adrenergic beta-Antagonists
Adrenergic Uptake Inhibitors
Aerosol Propellants
Affinity Labels
Agglutinins
Air Pollutants
Air Pollutants, Occupational
Air Pollutants, Radioactive
Alcohol Deterrents
Aldosterone Antagonists
Alkylating Agents
Amebicides
Anabolic Agents
Analgesics
Analgesics, Non-Narcotic
Analgesics, Opioid
Androgen Antagonists

Androgens
Anesthetics
Anesthetics, Combined
Anesthetics, Dissociative
Anesthetics, General
Anesthetics, Inhalation
Anesthetics, Intravenous
Anesthetics, Local
Angiogenesis Inducing Agents
Angiogenesis Inhibitors
Angiogenesis Modulating Agents
Angiotensin II Type 1 Receptor Blockers
Angiotensin-Converting Enzyme Inhibitors
Anion Exchange Resins
Antacids
Anthelmintics
Anti-Allergic Agents
Anti-Anxiety Agents
Anti-Arrhythmia Agents
Anti-Asthmatic Agents
Anti-Bacterial Agents
Anti-Dyskinesia Agents
Anti-HIV Agents
Anti-Infective Agents
Anti-Infective Agents, Local
Anti-Infective Agents, Urinary
Anti-Inflammatory Agents
Anti-Inflammatory Agents, Non-Steroidal
Anti-Obesity Agents
Anti-Retroviral Agents
Anti-Ulcer Agents
Antibiotics, Antifungal
Antibiotics, Antineoplastic
Antibiotics, Antitubercular
Anticarcinogenic Agents
Anticestodal Agents
Anticholesteremic Agents
Anticoagulants
Anticonvulsants
Antidepressive Agents
Antidepressive Agents, Second-Generation
Antidepressive Agents, Tricyclic
Antidiarrheals
Antidiuretic Agents
Antidotes
Antiemetics
Antifibrinolytic Agents
Antifoaming Agents
Antifungal Agents
Antihypertensive Agents
Antilipemic Agents
Antimalarials
Antimanic Agents
Antimetabolites
Antimetabolites, Antineoplastic
Antimitotic Agents
Antimutagenic Agents
Antinematodal Agents
Antineoplastic Agents
Antineoplastic Agents, Alkylating
Antineoplastic Agents, Hormonal
Antineoplastic Agents, Phytogenic
Antioxidants
Antiparasitic Agents
Antiparkinson Agents
Antiperspirants
Antiplatyhelmintic Agents
Antiprotozoal Agents
Antipruritics
Antipsychotic Agents
Antirheumatic Agents
Antisense Elements (Genetics)
Antisickling Agents
Antispermatogenic Agents
Antithyroid Agents
Antitreponemal Agents
Antitrichomonal Agents
Antitubercular Agents
Antitussive Agents
Antiviral Agents
Appetite Depressants
Appetite Stimulants
Aromatase Inhibitors
Astringents
Autonomic Agents
Biocompatible Materials
Blood Substitutes
Bone Cements
Bone Density Conservation Agents
Bronchoconstrictor Agents
Bronchodilator Agents
Buffers
Calcium Channel Agonists
Calcium Channel Blockers
Carbonic Anhydrase Inhibitors
Carcinogens
Carcinogens, Environmental
Cardiotonic Agents
Cardiovascular Agents
Cariogenic Agents
Cariostatic Agents
Cathartics
Caustics
Central Nervous System Agents
Central Nervous System Depressants
Central Nervous System Stimulants
Chelating Agents
Chemical Warfare Agents
Chemosterilants
Cholagogues and Choleretics
Cholinergic Agents
Cholinergic Agonists
Cholinergic Antagonists
Cholinesterase Inhibitors
Cholinesterase Reactivators
Chromogenic Compounds
Coagulants
Coccidiostats
Coloring Agents
Complement Inactivating Agents
Complex Mixtures
Contraceptive Agents
Contraceptive Agents, Female
Contraceptive Agents, Male
Contraceptives, Oral
Contraceptives, Oral, Combined
Contraceptives, Oral, Hormonal
Contraceptives, Oral, Sequential
Contraceptives, Oral, Synthetic
Contraceptives, Postcoital
Contraceptives, Postcoital, Hormonal
Contraceptives, Postcoital, Synthetic
Contrast Media
Convulsants
Cosmetics
Cross-Linking Reagents
Cryoprotective Agents
Culture Media
Cyclooxygenase 2 Inhibitors
Cyclooxygenase Inhibitors
Cysteine Proteinase Inhibitors
Cytotoxins
Defoliants, Chemical
Delayed-Action Preparations
Dental Disinfectants
Dental Materials
Dermatologic Agents
Dermotoxins
Detergents
Dialysis Solutions
Dipeptidyl-Peptidase IV Inhibitors
Disinfectants
Diuretics
Diuretics, Osmotic
Dopamine Agents
Dopamine Agonists
Dopamine Antagonists
Dopamine Uptake Inhibitors
Drug Carriers

Emetics
Emollients
Endocannabinoids
Endothelium-Dependent Relaxing Factors
Environmental Pollutants
Enzyme Activators
Enzyme Inhibitors
Enzyme Reactivators
Estradiol Antagonists
Estrogen Antagonists
Estrogen Receptor Modulators
Estrogens
Estrogens, Non-Steroidal
Excipients
Excitatory Amino Acid Agents
Excitatory Amino Acid Agonists
Excitatory Amino Acid Antagonists
Expectorants
Explosive Agents
Fat Substitutes
Fatty Acid Synthesis Inhibitors
Fertility Agents
Fertility Agents, Female
Fertility Agents, Male
Fertilizers
Fibrin Modulating Agents
Fibrinolytic Agents
Filaricides
Fixatives
Flavoring Agents
Fluorescent Dyes
Folic Acid Antagonists
Food Additives
Food Coloring Agents
Food Preservatives
Free Radical Scavengers
Fungicides, Industrial
GABA Agents
GABA Agonists
GABA Antagonists
GABA Modulators
Ganglionic Blockers
Ganglionic Stimulants
Gastrointestinal Agents
Glucocorticoids
Glycine Agents
Gout Suppressants
Growth Inhibitors
Growth Substances
GTP Phosphohydrolase Activators
Hallucinogens
Hazardous Substances
Hemagglutinins
Hematinics
Hematologic Agents
Hemolytic Agents
Hemostatics
Heparin Antagonists
Herbicides
Histamine Agents
Histamine Agonists
Histamine Antagonists
Histamine H1 Antagonists
Histamine H1 Antagonists, Non-Sedating
Histamine H2 Antagonists
Histamine H3 Antagonists
HIV Fusion Inhibitors
HIV Protease Inhibitors
Hormone Antagonists
Hormones
Hormones, Hormone Substitutes, and Hormone Antagonists
Hydroxymethylglutaryl-CoA Reductase Inhibitors
Hypnotics and Sedatives
Hypoglycemic Agents
Immunologic Factors
Immunosuppressive Agents
Immunotoxins
Incretins
Indicators and Reagents
Insect Repellents
Insecticides
Insulin Antagonists
Intercalating Agents
Interferon Inducers
Ion Exchange Resins
Ionophores
Iron Chelating Agents
Irritants
Keratolytic Agents
Leprostatic Agents
Leukotriene Antagonists
Lipotropic Agents
Lipoxygenase Inhibitors
Luminescent Agents
Luteolytic Agents
Membrane Transport Modulators
Menstruation-Inducing Agents
Micronutrients
Mineralocorticoids
Miotics
Mitogens
Mitosis Modulators
Molecular Probes
Molluscacides
Monoamine Oxidase Inhibitors
Mouthwashes
Muscarinic Agonists
Muscarinic Antagonists
Muscle Relaxants, Central
Mutagens
Mydriatics
Myeloablative Agonists
Narcotic Antagonists
Narcotics
Nasal Decongestants
Natriuretic Agents
Neuromuscular Agents
Neuromuscular Blocking Agents
Neuromuscular Depolarizing Agents
Neuromuscular Nondepolarizing Agents
Neuroprotective Agents
Neurotoxins
Neurotransmitter Agents
Neurotransmitter Uptake Inhibitors
Nicotinic Agonists
Nicotinic Antagonists
Nitric Oxide Donors
Nootropic Agents
Noxae
Nucleic Acid Synthesis Inhibitors
Ointment Bases
Oligodeoxyribonucleotides, Antisense
Oligonucleotides, Antisense
Ophthalmic Solutions
Oxidants
Oxidants, Photochemical
Oxytocics
Parasympatholytics
Parasympathomimetics
Peripheral Nervous System Agents
Peroxisome Proliferators
Pesticide Synergists
Pesticides
Pharmaceutic Aids
Pharmaceutical Solutions
Phosphodiesterase Inhibitors
Photoaffinity Labels
Photosensitizing Agents
Phytoestrogens
Plant Growth Regulators
Plasma Substitutes
Plasticizers
Platelet Aggregation Inhibitors
Poisons
Potassium Channel Blockers
Preservatives, Pharmaceutical
Progestins
Prostaglandin Antagonists
Protease Inhibitors
Protective Agents
Protein Kinase Inhibitors
Protein Synthesis Inhibitors
Psychotropic Drugs
Pulmonary Surfactants
Pyrogens

Radiation-Protective Agents
Radiation-Sensitizing Agents
Radioactive Pollutants
Radiopharmaceuticals
Reducing Agents
Renal Agents
Reproductive Control Agents
Resins, Synthetic
Respiratory System Agents
Reverse Transcriptase Inhibitors
Riot Control Agents, Chemical
Rodenticides
Schistosomicides
Sclerosing Solutions
Selective Estrogen Receptor Modulators
Sensory System Agents
Serine Proteinase Inhibitors
Serotonin Agents
Serotonin Agonists
Serotonin Antagonists
Serotonin Uptake Inhibitors
Siderophores
Sodium Channel Blockers
Sodium Chloride Symporter Inhibitors
Sodium Potassium Chloride Symporter Inhibitors
Soil Pollutants
Solvents
Spermatocidal Agents
Sulfhydryl Reagents
Sunscreening Agents
Surface-Active Agents
Surgical Fixation Devices
Sweetening Agents
Sympatholytics
Sympathomimetics
Tear Gases
Teratogens
Tissue Adhesives
Tocolytic Agents
Toothpaste
Trace Elements
Tranquilizing Agents
Trypanocidal Agents
Trypsin Inhibitors
Tubulin Modulators
Uncoupling Agents
Uricosuric Agents
Vasoconstrictor Agents
Vasodilator Agents
Vehicles
Vitamin B Complex
Vitamins
Water Pollutants, Chemical

MeSH does include a tool for indexers to help them determine which pharmacological actions apply to a given drug. These are essentially long lists of the all drugs that fall into a particular *pharmacological action* category. The list includes both MeSH headings and non-headings:

Analgesics
[Pharmacological Action]
:
Antipyrine (MeSH Term)
Apazone (MeSH Term)
Arteparon (Substance Name)
Arthrotec (Substance Name)
Aspirin (MeSH Term)
azulene (Substance Name)
B 4162 (Substance Name)
baicalin (Substance Name)
:

Fibrinolytic Agents
[Pharmacological Action]
:
Ancrod (MeSH Term)
Anistreplase (MeSH Term)
aprosulate (Substance Name)
ardeparin (Substance Name)
asarone (Substance Name)
Aspirin (MeSH Term)
Batroxobin (MeSH Term)
benzarone (Substance Name)
Brinolase (MeSH Term)
:

Anti-Inflammatory Agents, Non-Steroidal
[Pharmacological Action]
:
antiflammin P2 (Subst. Name)
Antipyrine (MeSH Term)
Apazone (MeSH Term)
Arteparon (Substance Name)
Arthrotec (Substance Name)
Aspirin (MeSH Term)
azulene (Substance Name)
baicalin (Substance Name)
balsalazide (Substance Name)
:

Analgesics, Non-Narcotic
[Pharmacological Action]
:
Apazone (MeSH Term)
Arteparon (Substance Name)
Arthrotec (Substance Name)
Aspirin (MeSH Term)
azulene (Substance Name)
baicalin (Substance Name)
balsalazide (Substance Name)
:

Cyclooxygenase Inhibitors [Pharmacological Action]
:
4,5-Dihydro-1-(3-(trifluoromethyl)phenyl)-1H-pyrazol-3-amine (MeSH Term)
4-(5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl) benzenesulfonamide (Substance Name)
acetylsalicylic acid lysinate (Substance Name)
Aspirin (MeSH Term)
celecoxib (Substance Name)
Diclofenac (MeSH Term)
:

Here are several records that illustrate the actual indexing assigned to papers about aspirin. Only the drug and pharmacological headings are shown. Note that the fourth paper (*Effects of aspirin during exercise ...)* does was not assigned a pharmacological action heading. Even indexers make mistakes!

Record 1

TI: Aspirin for the primary prevention of cardiovascular events in women and men: a sex-specific meta-analysis of randomized controlled trials.

SO: JAMA. 2006 Jan 18; 295(3): 306-13

Major MeSH:

- Aspirin/therapeutic use;
- Platelet Aggregation Inhibitors/therapeutic use

Minor MeSH:

- Aspirin/adverse effects
- Platelet Aggregation Inhibitors/adverse effects

Record 2

TI: Sex differences in platelet reactivity and response to low-dose aspirin therapy.

SO: JAMA. 2006 Mar 22; 295(12): 1420-7

Major MeSH:

- Aspirin/therapeutic use;
- Cyclooxygenase Inhibitors/therapeutic use;
- Platelet Aggregation Inhibitors/therapeutic use

Minor MeSH:

- Aspirin/pharmacology
- Cyclooxygenase Inhibitors/pharmacology
- Platelet Aggregation Inhibitors/pharmacology

Record 3

TI: A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women.

SO: N Engl J Med. 2005 Mar 31; 352(13): 1293-304

Major MeSH:

- Aspirin/therapeutic use;
- Platelet Aggregation Inhibitors/therapeutic use

Minor MeSH:

- Anti-Inflammatory Agents, Non-Steroidal/therapeutic use
- Aspirin/administration and dosage
- Aspirin/adverse effects
- Cyclooxygenase Inhibitors/therapeutic use
- Platelet Aggregation Inhibitors/administration and dosage
- Platelet Aggregation Inhibitors/adverse effects

Record 4

TI: Effects of aspirin during exercise on the incidence of high-altitude headache: a randomized, double-blind, placebo-controlled trial.

SO: Headache. 2001 Jun; 41(6): 542-5

Major MeSH:

- Aspirin/therapeutic use

Minor MeSH:

Record 5

TI: Efficacy and safety of metamizol vs. acetylsalicylic acid in patients with moderate episodic tension-type headache: a randomized, double-blind, placebo- and active-controlled, multicentre study.

SO: Cephalalgia. 2001 Jun; 21(5): 604-10

Major MeSH:

- Analgesics, Non-Narcotic/therapeutic use;
- Anti-Inflammatory Agents, Non-Steroidal/therapeutic use;
- Aspirin/therapeutic use;
- Dipyrone/therapeutic use

Minor MeSH:

- Analgesics, Non-Narcotic/adverse effects
- Anti-Inflammatory Agents, Non-Steroidal/administration and dosage
- Anti-Inflammatory Agents, Non-Steroidal/adverse effects
- Aspirin/adverse effects
- Dipyrone/administration and dosage
- Dipyrone/adverse effects