


Session 6 Drugs Affecting Body Defences

6.1 Tutorial Activity: students develop tables or flow diagrams to determine the drug treatments of rheumatoid arthritis and gout. Discuss your flow chart with your peers. A suggested tabular format has been given below but you are encouraged to do your own flow chart or other formats.

Pathophysiology of the of inflammatory joint diseases and gout given in an information sheet (6.3 below)

6.2 DRUG DIARY – Please use your Textbook and Reading Guide for information about weekly compilation of a Drug Booklet, with summaries on major classes of drugs, assessed on the final examination (Parts A and B) and the Minimonographs Assignment (Assignment 2). Your Drug Booklet is also called a drug diary (you start it each week in the tutorial, and are encouraged to finish it that week in your private study time or to finish all entries in the Study Weeks).

Also refer to your handout BIOP211_SN06-12_TutorialPeerReview_Minimonograph.pdf, available from the Endeavour LMS Website, for a summary of the majority of the pharmacology topics.

 The following can be included in your Drug Mini-monograph assignment or could be on the final exam:

Discuss these medications that work on Immune Responses or similar. 10 marks for (i) examples (ii) indications (iii) mechanism of action (iv) efficacy and limitations or cautions / contra-indications (v) adverse effects. Mark your own answers using the Pharmacology text or online resources. Alternatively, peer review each other's answers, allocating 10 marks per drug class:

- Non-selective COX inhibitors
- Selective COX inhibitors
- DMARDs (disease-modifying anti-rheumatic drugs)
- Corticosteroids to treat muskulo-skeletal diseases e.g. RA (rheumatoid arthritis)
- Anti-gout drugs, both prophylactics and those needed to treat the acute attacks

Table 6.1 Suggested tabular format for Drug Diary entries listed by Indication – Gout and RA

Gout	Indicated when NSAIDs contra/i	Chronic Gout & hyperuricaemia	Prevents recurrent gout attacks	NSAIDs	Corticosteroids
Drug & Drug Class					
Pharmaco-dynamics					
Pharmaco-kinetics					
ADR					

Gout	Indicated when NSAIDs contra/i	Chronic Gout & hyperuricaemia	Prevents recurrent gout attacks	NSAIDs	Corticosteroids
Interactions					
Warnings & Contra-indications					
Rheumatoid Arthritis, RA	DMARD = disease modifying anti-rheumatic drug	Mod to severe RA unresponsive to other treatments	RA, Crohn's disease (inflammatory bowel disease), ankylosing spondylitis		NSAID and steroidal anti-inflammatories
Drug & Drug Class	Auranofin & aurothiomalate (Gold Salts) - DMARD	Penicillamine, DMARD	Infliximab, DMARD	Anakinra, cytokine modulator, biological DMARD	See above for indomethacin & hydrocortisone
Pharmacodynamics					
Pharmacokinetics					
ADR					
Interactions					
Warnings contra-indications					

6.1 Answer True or False to these questions. Use your textbook. Feedback is available in Review Quiz 6



1. Leflunomide is a DMARD that is recirculated through the liver. After ceasing therapy it may take as long as 2 years to become undetectable in the blood.
2. The gingival hyperplasia caused by cyclosporins is an irreversible adverse reaction
3. Inhibition of cyclo-oxygenase-2 (COX-2) can induce gastric ulceration.
4. Gold salts suppress the phagocytic action of macrophages and leucocytes.
5. Glucosamine, an over-the-counter product available from health food stores, has been shown to be helpful in treating osteoarthritis.
6. Stimulation of H1 and H2 receptors can result in hypertension.

6.2 Choose the best response to these questions. Use your textbook or flow diagram (data table) compiled below on the drugs used to treat rheumatoid arthritis. Feedback is available in Review Quiz 6

Cloze Exercises done on Endeavour LMS require you to get spelling and acronyms accurate. This is good preparation for your assignment writing skills.

Choose your answers from this list:

I; II; III; IV; a non-steroid anti-inflammatory drug, NSAID; allopurinol; colchicine; gold salts; leflunomide; methotrexate; non-selective; paracetamol; selective; xanthine oxidase

In the case of a person who presents with an inflamed first metatarsal-phalangeal joint and skin desquamation off the area over the first MTP, that flared up six months ago, went away and has now come back, and got worse over the past few days, this person would be advised to take _____

There is a drug that is an antidote in heavy-metal poisoning, and is also a DMARD of unknown mechanism of action. It is noted that while on this drug the levels of circulating immune _____ complexes is reduced, but how these complexes are involved in rheumatoid arthritis is also unknown.

As a prophylactic to prevent acute attacks of gout from occurring in this person once their acute attack has cleared, the person would probably be prescribed _____

This drug for prophylaxis, in people with gout and hyperuricaemia, inhibits the actions of _____

A drug that has been in the records as having been used to treat gout for about four hundred years is _____ and though having been in use for a long time, its mechanism of action is still being investigated

In natural healing clinics, some clients may not be on the commonest Disease Modifying Antirheumatic drugs, DMARDS, so it is important for these practitioners to know how to find out about the mechanisms of action of newer immunosuppressants such as {1:SHORTANSWER:=leflunomide} which targets cytosine, C, thymine, T, and uracil, U production in T-lymphocytes and B-lymphocytes. Knowing its mechanism of action, natural healers can then understand its most serious adverse effect which would be pancytopenia.

Another DMARD in use for centuries and similarly, for which the mechanism of action possibly inside macrophages, is still being investigated, is _____

The DMARD that inhibits the production of tetrahydrofolate, from dihydrofolate, in a reaction that makes the coenzyme gain two hydrogen atoms, is the drug _____



Celecoxib is a _____ cyclo-oxygenase-2 inhibitor but it is still under phase IV pharmacovigilance and a “black box” by the Therapeutic Goods Administration, TGA, in Australia, and MedSafe in New Zealand <http://www.medsafe.govt.nz/profs/adverse/minutescox2.htm>

A drug which is analgesic but will not be able to treat major inflammation only minor inflammation and mild pain, such as in tooth removal, and is only a first-line treatment of osteoarthritis and arthritis towards the goal of maintaining functional use, is _____

6.2 Develop a flow diagram.

Anti-Inflammatory drugs including Steroids

Develop/design a table or flow diagram to determine the drug treatments of Rheumatoid Arthritis and Gout. Include in this the name of the drug class and name, pharmacodynamics, pharmacokinetics, adverse reactions, drug interactions and warnings & contraindications

6.3 HANDOUT FOR SESSION 6 Pathophysiology of the Inflammatory Joint Diseases & Gout

PATHOPHYSIOLOGY OF INFLAMMATORY JOINT DISEASES AND GOUT

There are many conditions that cause inflammation of the joints. These include:

1. Rheumatoid arthritis
2. Psoriatic arthritis
3. Soft tissue injury
4. Septic/infective Arthritis
5. Ankylosing spondylitis
6. Gout/Pseudogout
7. Reactive arthritis

Rheumatoid Arthritis

An inflammatory arthritis in which joints, usually including those of the hands and feet, are inflamed, resulting in swelling, pain and often destruction of joints.

It is an autoimmune disease where components of the immune system (cell and humoral mediated) attack the soft and connective tissue within the body. It is characterised by increased levels of immunoglobulins (IgG, IgA, IgM) and autoantibodies (RF) in the blood. Immune complexes form in the intra-articular cavity and a Type III hypersensitivity develops. This type II hypersensitivity leads to:



- platelet aggregation and degranulation with microthrombus formation and vasoactive amine release;
- Complement is activated and the complexes are phagocytosed resulting in destruction of cartilage, bone and ligaments of the joints;
- causing deformity, formation of the pannus (over-proliferation of cells), instability and scarring.

Psoriatic Arthritis

Joint inflammation in people who have psoriasis.

Similar to Rheumatoid arthritis however there are no antibodies present (hence the term RF negative – rheumatoid factor negative arthritis).

Septic/Infective Arthritis

Result from haematogenous spread of microbes or as a complication of an infection in adjacent soft tissue or by direct introduction of micro-organisms directly into the joint as a result of a penetrating injury (cortisone injection) or surgical procedure (arthroscopy)

May be caused by viral, bacterial or fungal infection.

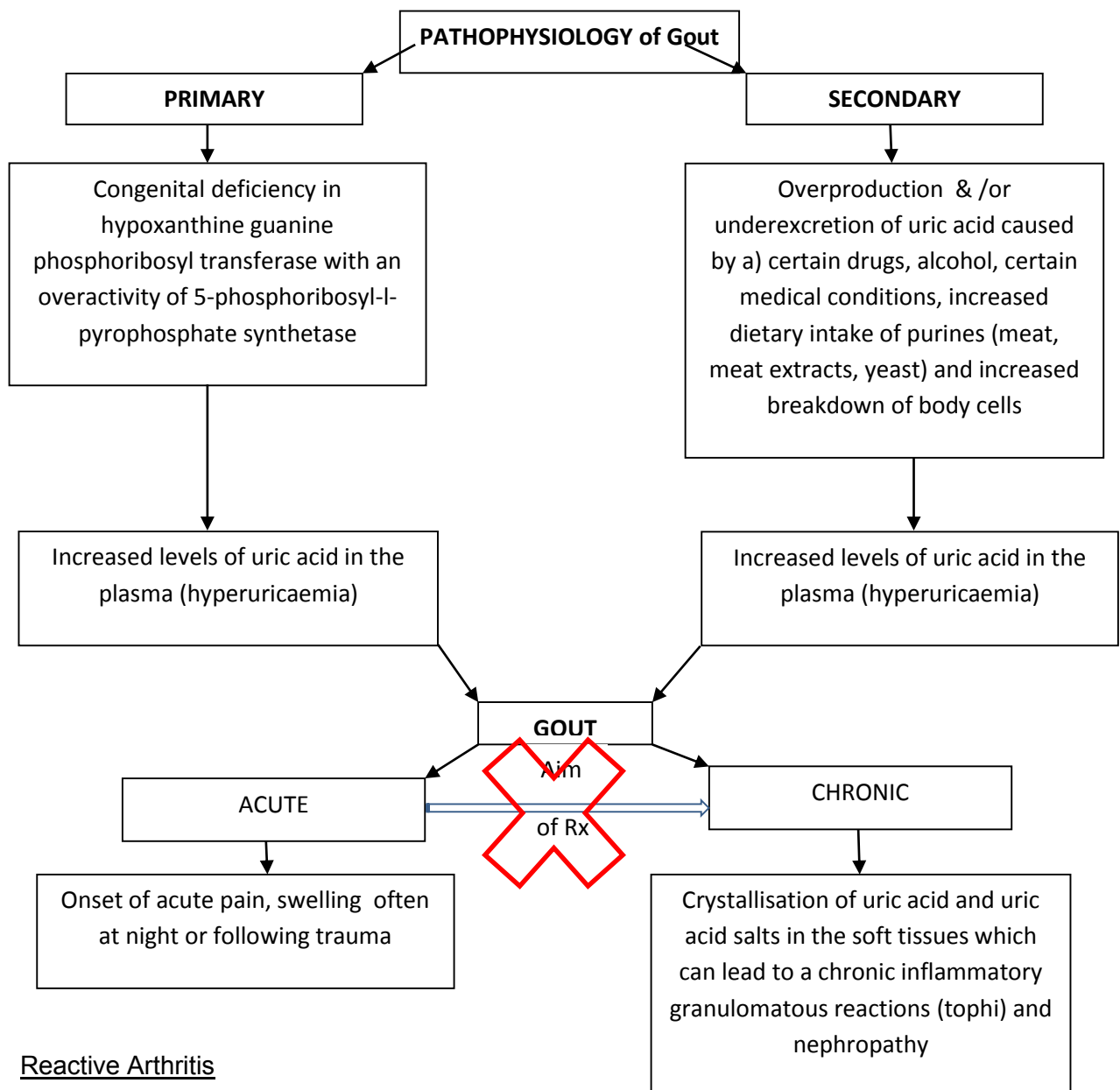
Ankylosing Spondylitis

Chronic inflammation of the axial skeleton (spine) but can also affect the shoulders and lower limb joints

Linked to HLA- B27 and CD* T cells where there is inflammation in the enthesis (where ligaments attach to bones) which then leads to bony ankylosis of the joint periphery and central endochondral ossification. This progresses to calcification with the production of a bony bridge between the vertebral bodies (syndesmophyte) and results in a bony rigidity of the spine.

Gout

Metabolic disease characterised by deposition of urate crystals in and around joints and often associated with hyperuricaemia.



Reactive Arthritis

A sterile synovitis which occurs following an infection such as dysentery or a sexually acquired infection.

There is an increased susceptibility to bacterial persistence due to the presence of HLA-B27.

Bibliography

Beers, M (Ed) 2003, *The Merck manual of medical information*, Pocket Books , New York

Kumar, P & Clark M 2013, *Clinical medicine* 8th Edition, Saunders Elsevier, Edinburgh

Vardaxis, N 2010, *A textbook of pathology*, Mosby Elsevier, Sydney

Readings

Use the Reading Guide to locate sections in the text.


Revision Questions / Activities from the Reading Guide

1. Describe the mechanism of action of NSAIDs (non-s_____ anti-_____ drugs)
2. What is the benefit of selective COX II inhibitors? (C_____ -o_____ ase II Inhibitors)
3. Name 6 different classes of NSAIDs.
4. Outline the major adverse effect of NSAIDs and explain the rationale behind why this happens.
5. List 3 contraindications & warnings involved with the use of NSAIDs
6. Compare and contrast aspirin and paracetamol (include M of A, indications, adverse effects, contraindications).
7. Outline how aspirin exerts its anticoagulant/antiplatelet effect.
8. What are the 2 properties that corticosteroids exhibit?
9. Corticosteroids have many adverse effects. Name 5.
10. Outline the advantages that DMARDs have over other drugs used in the treatment of RA. D_____ -m_____ anti-_____ drugs. R_____ A_____ -itis.
11. What drugs are used in an acute attack of gout?
12. What drugs are used to prevent subsequent attacks of gout?

Answer the following:

From Bryant & Knights (2011; 2015)

- Review questions: Drugs Affecting Body Defences: Anti-inflammatory & Immunomodulating Drugs. Especially questions reviewing the inflammatory response, complement, allergic (hypersensitivity) reactions, hyperuricaemia, probenecid

 From subject website, review quiz, Students discuss their "Drug Diaries" in class or in on-line forums, and compile a Class/ Cohort Flow Chart / Table of Drug Treatments in RA and gout