Therapeutic areas – Part 1

Inflammation & Immunology

Module 4 Topic 4_2

Pain

- An unpleasant sensation usually associated with tissue damage
- Chemicals like prostaglandins, histamine etc. released following tissue damage stimulate the pain receptors
- Pain sensation transmitted via spinal cord to ***thalamus*** and cerebral cortex

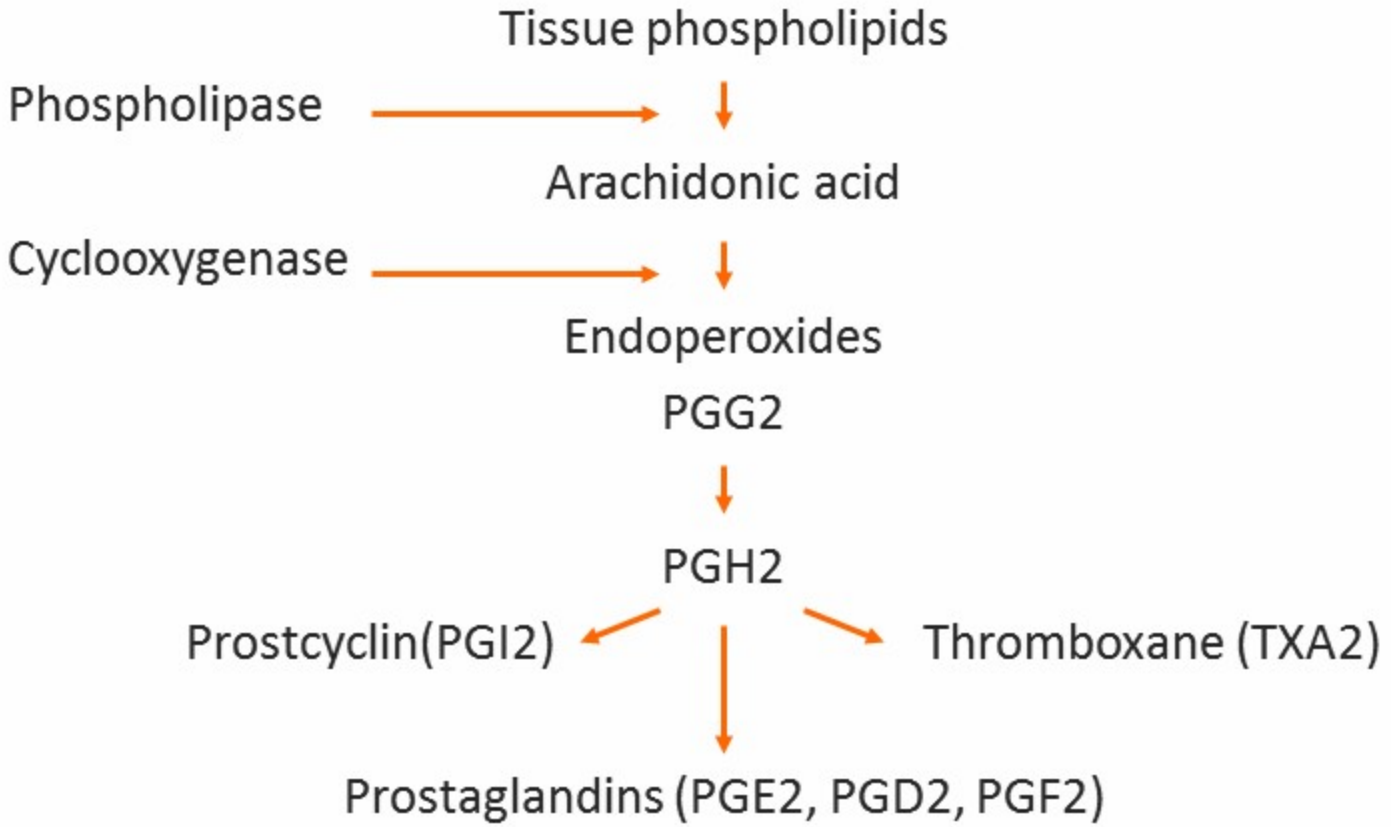
Inflammation

- Response of living tissue to injury
- Injury may be due to
  - Physical agents
  - Chemical agents
  - Microorganisms
  - Immunological

Inflammation

- Pathophysiology
  - Increase in the local blood flow
  - Outpouring of fluid from the capillaries
  - Migration of leukocytes (WBCs) into the tissue
- Chemical mediators of inflammation
  - Arachidonic acid derivatives – PG, leukotrienes
  - Histamine
  - Bradykinin

Inflammation



Inflammation

- Actions of Prostaglandins
  - Dilatation of small blood vessels by PGI2, vasoconstriction by TXA2
  - Inhibition of platelet aggregation by PGI2, promotion of platelet aggregation by TXA2
  - PGEs contract or relax smooth muscles
  - PGEs & PGI2 inhibit gastric acid secretion
  - PG influence salt & water excretion by kidneys
  - PGs mediate inflammatory changes by actions on blood vessels (redness, swelling) & nerve endings (pain)

Inflammation

- Signs of inflammation
  - **Pain** (dolor)
  - **Redness** (rubor)
  - **Local heat** (calor)
  - **Swelling** (tumor)
  - **Loss of function** (functio laesa)

Inflammatory Disorders

- ***Rhinitis*** – inflammatory disorder of nose
- ***Sinusitis*** - inflammatory disorder of air sinuses
- ***Pharyngitis*** - inflammatory disorder of pharynx
- ***Bronchitis*** - inflammatory disorder of bronchi
- ***Gastroenteritis*** - inflammatory disorder affecting gastro-intestinal tract

Inflammatory Disorders

- ***Hepatitis*** - inflammatory disorder of liver
- ***Pancreatitis*** - inflammatory disorder of pancreas
- ***Nephritis*** - inflammatory disorder of kidneys
- ***Cystitis*** - inflammatory disorder of urinary bladder
- ***Osteomyelitis*** - inflammatory disorder of bone and bone marrow
- ***Encephalitis*** - inflammatory disorder of brain tissue
- ***Neuritis*** - inflammatory disorder of a nerve

Inflammatory Disorders

- Arthritis - inflammatory disorder of a joint
  - Rheumatoid arthritis
  - Osteoarthritis
- Spondylitis - inflammatory disorder of vertebra
- Soft tissue inflammations -
  - Bursitis - inflammatory disorder of a bursa
  - Tenosynovitis – inflammation of tendons & their synovial sheaths
  - Sprain
  - Lumbago
  - Sciatica
- Dental inflammatory conditions

Management of Pain

- **Management of Pain**
  - Narcotic Analgesics e.g. morphine, codeine, pethidine
  - Non-narcotic Analgesics e.g. paracetamol

Management of Pain

- **Paracetamol**
  - Derivative of phenacetin
  - V good ***analgesic*** and ***antipyretic*** effect
  - Potent inhibitor of PG synthesis in CNS
  - Rapid & complete absorption from GI tract
  - Tmax 10 to 60 min, t1/2 1 to 3 hrs
  - Plasma protein binding negligible
  - Metabolized in liver, metabolites excreted in urine
  - Safe & well tolerated
  - Dosage: adults – 325 mg to 1 g up to 4 times a day (max 4 g); children – 40 to 480 mg up to 5 times a day

Management of Inflammatory Disorders

- **Management of inflammatory disorders**
  - Anti-inflammatory drugs
    - Corticosteroids
    - Non-steroidal anti-inflammatory drugs (NSAIDs)

Management of Inflammatory Disorders

- Non-steroidal Anti-Inflammatory Drugs (NSAIDs)
  - Salicylic acid derivatives e.g. aspirin
  - Propionic acid derivatives e.g. ibuprofen
  - Acetic acid derivatives e.g. diclofenac
  - Indole acetic acid derivatives e.g. indomethacin
  - Oxicams e.g. piroxicam
  - Anthranilic acid derivatives e.g. mefenamic acid

Management of Inflammatory Disorders

- **Non-steroidal Anti-Inflammatory Drugs (NSAIDs)**
  - Mechanism of Action
    - Inhibition of enzyme 'cyclooxygenase'
    - Prostaglandin synthesis blocked
    - Relief from pain, redness and swelling

Immune system

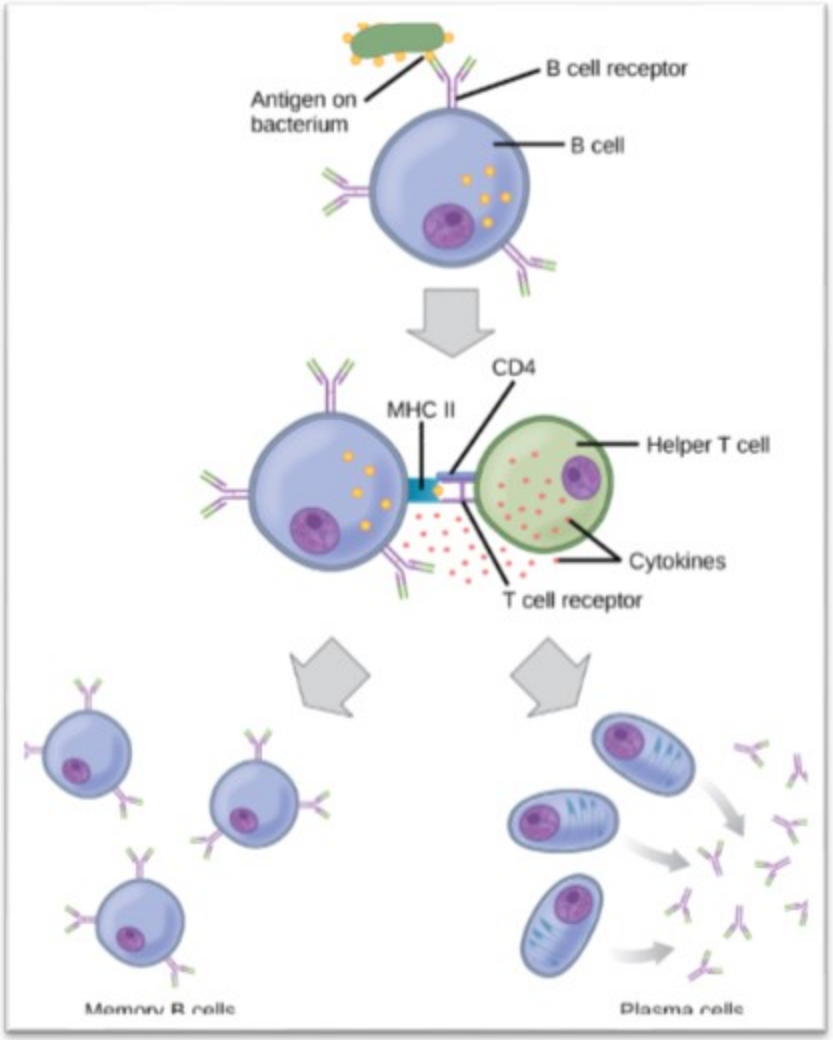
- **First line of defense** – skin (nonspecific defense)
- **Second line of defense** - inflammatory response
- **Adaptive immune system** - "remembers" the antigen / pathogen, allowing for a faster response on next exposure

Immune system

Humoral immunity

Activated B cells grow rapidly

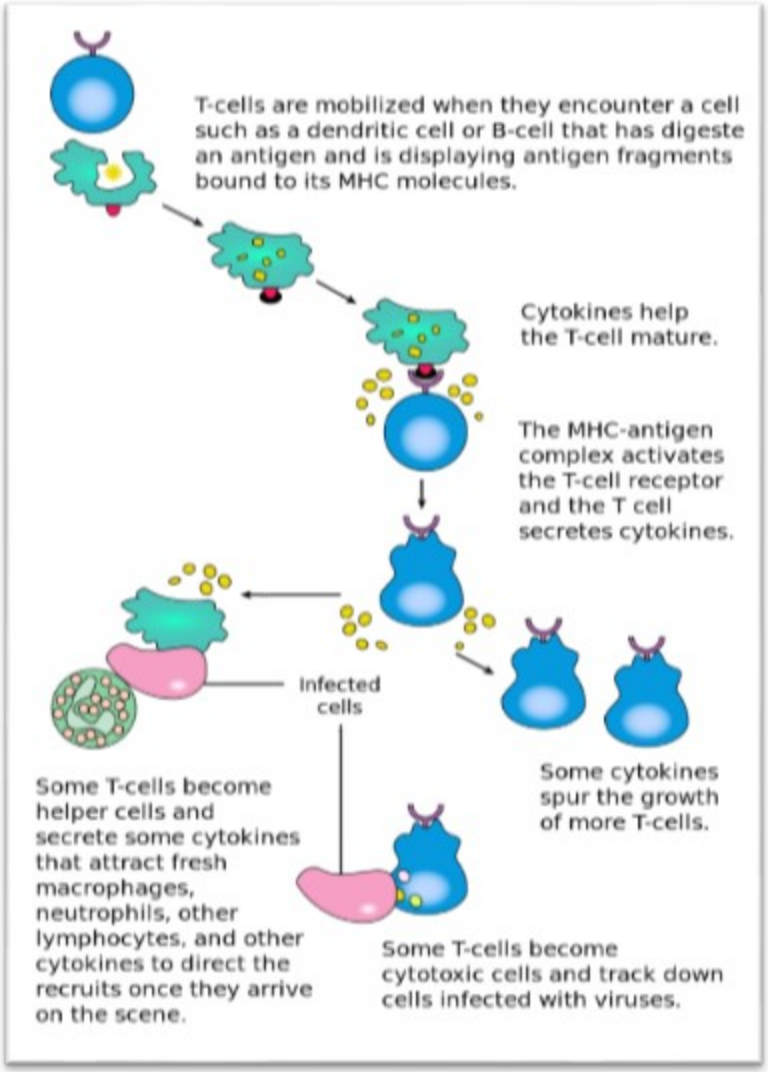
- producing **plasma cells**, which release antibodies into the bloodstream
- and **memory B cells**



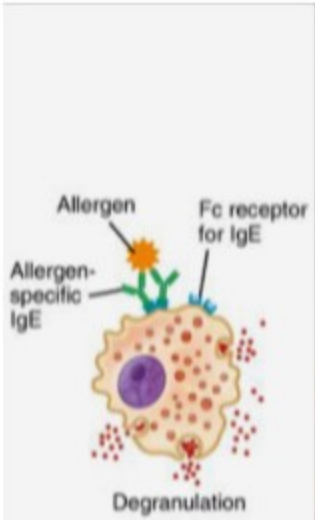
Immune system

Cell-mediated immunity

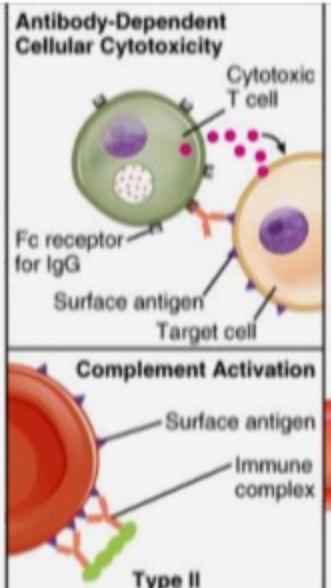
- **Killer T cells** (cytotoxic T cells) assist with the elimination of infected body cells by releasing toxins into them and promoting **apoptosis**
- **Helper T cells** act to activate other immune cells



Types of allergic reactions



Type I



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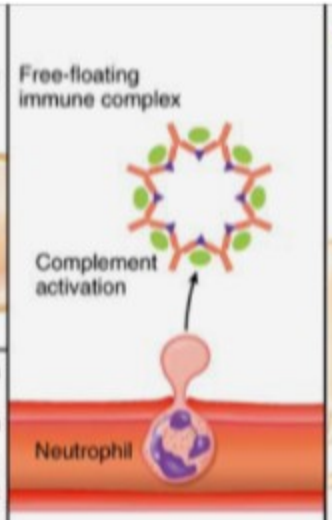
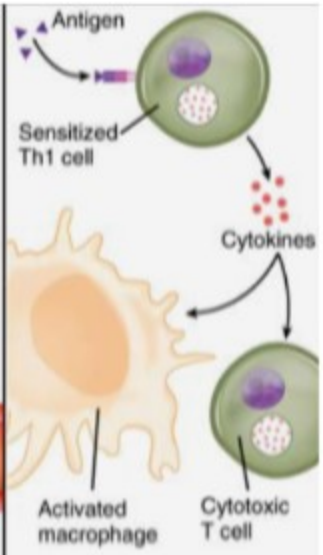


Type III



Type IV

IgE-Mediated Hypersensitivity	IgG-Mediated Cytotoxic Hypersensitivity	Immune Complex-Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
IgE is bound to mast cells via its Fc portion. When an allergen binds to these antibodies, crosslinking of IgE induces degranulation.	Cells are destroyed by bound antibody, either by activation of complement or by a cytotoxic T cell with an Fc receptor for the antibody (ADCC)	Antigen–antibody complexes are deposited in tissues, causing activation of complement, which attracts neutrophils to the site	Th1 cells secrete cytokines, which activate macrophages and cytotoxic T cells and can cause macrophage accumulation at the site
Causes localized and systemic anaphylaxis, seasonal allergies including hay fever, food allergies such as those to shellfish and peanuts, hives, and eczema	Red blood cells destroyed by complement and antibody during a transfusion of mismatched blood type or during erythroblastosis fetalis	Most common forms of immune complex disease are seen in glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus	Most common forms are contact dermatitis, tuberculin reaction, autoimmune diseases such as diabetes mellitus type I, multiple sclerosis, and rheumatoid arthritis

CNS Disorders

Dementia (contd)

- **Prevention**
  - **Get enough vitamin D** - People with low blood levels of vitamin D are more likely to develop Alzheimer's disease and other forms of dementia
  - **Control of blood pressure**
  - **Maintain a healthy diet** - Eating a healthy diet rich in fruits, vegetables, whole grains and omega-3 fatty acids, commonly found in certain fish and nuts might lower risk of dementia

CNS Disorders

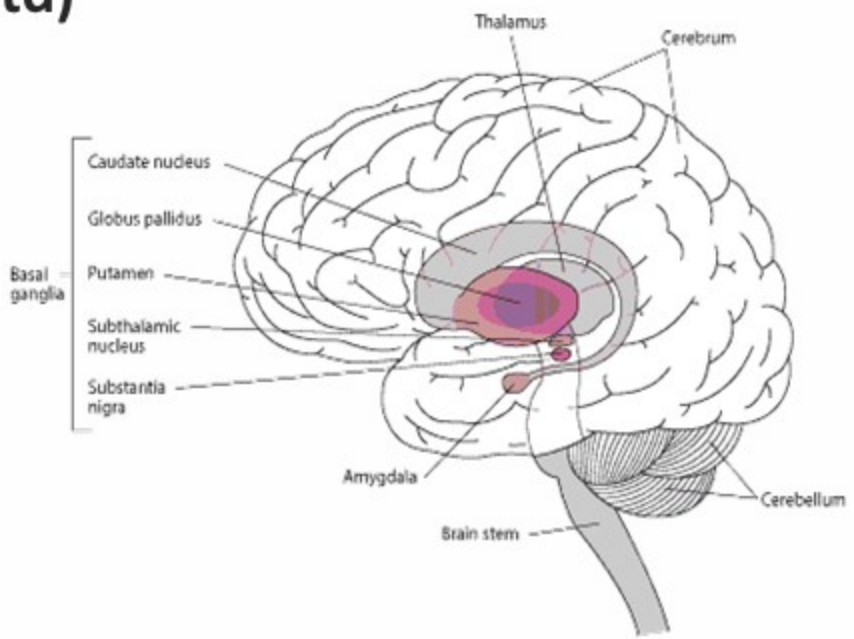
Parkinson's Disease (PD)

- A slowly progressive, degenerative disorder characterized by resting tremor, stiffness (rigidity), slow and decreased movement (bradykinesia), and gait and/or postural instability
- **Pathologic hallmark of PD** is synuclein-filled Lewy bodies in the nigrostriatal system

CNS Disorders

Parkinson's Disease (contd)

- Pigmented neurons of the substantia nigra, locus ceruleus, and other brain stem dopaminergic cell groups degenerate, leading to depletion of dopamine and causes many of the motor manifestations of PD



CNS Disorders

Parkinson's Disease (contd)

- Treatment
  - Carbidopa/levodopa (mainstay of treatment)
  - Amantadine, MAO type B (MAO-B) inhibitors e.g. selegiline, or, in few patients, anticholinergic drugs e.g. benztropine, diphenhydramine
  - Dopamine agonists e.g. ropinirole
  - Catechol *O*-methyltransferase (COMT) inhibitors, always used with levodopa, particularly when response to levodopa is wearing off
  - Surgery if drugs do not sufficiently control symptoms or have intolerable adverse effects