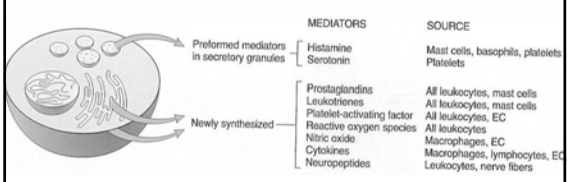
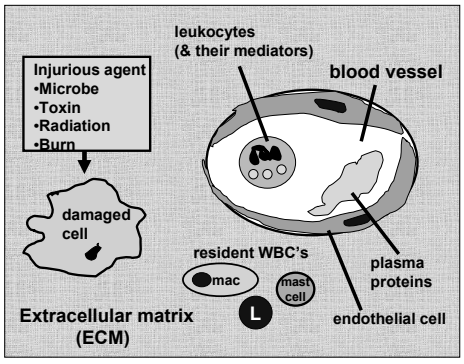
Inflammation 2:

1. Chemical mediators
2. Systemic effects
3. Chronic inflammation

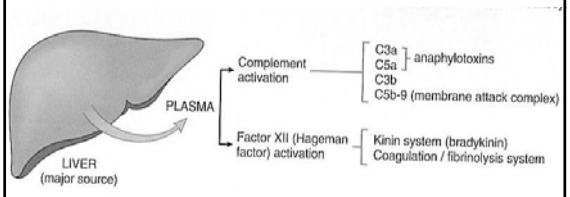
Cell-Derived Mediators



Key Players in Inflammation



Plasma Protein-Derived Mediators



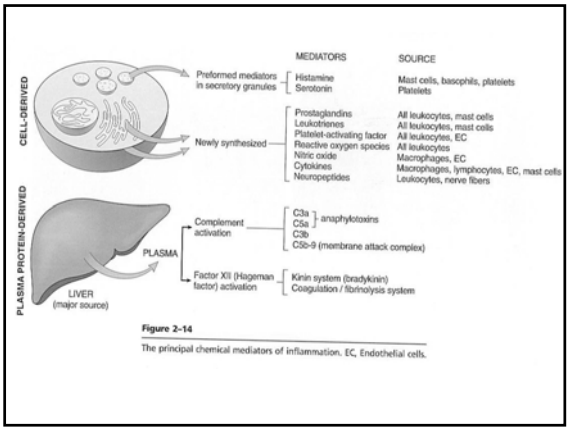
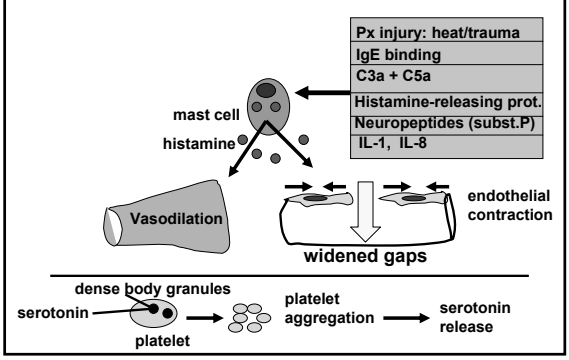
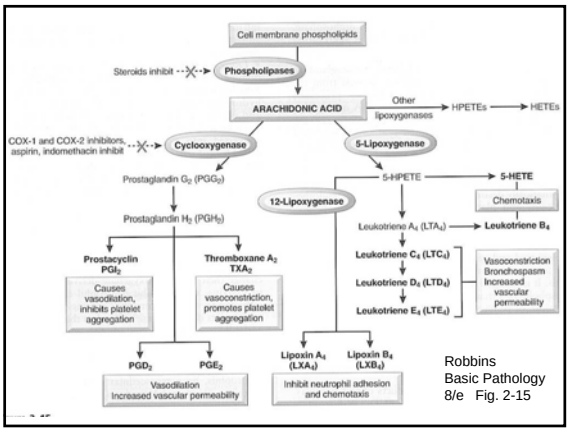


Figure 2–14
The principal chemical mediators of inflammation. EC, Endothelial cells.

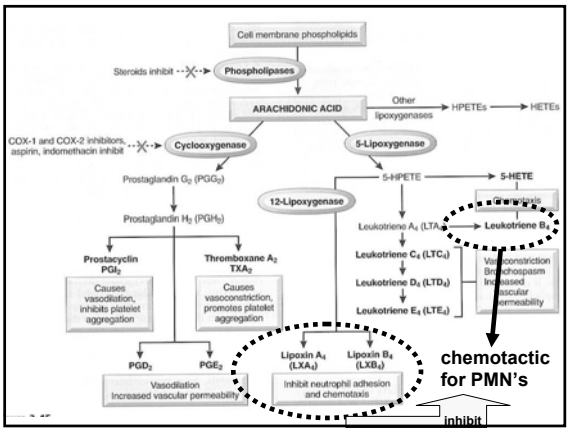
Vasoactive Amines

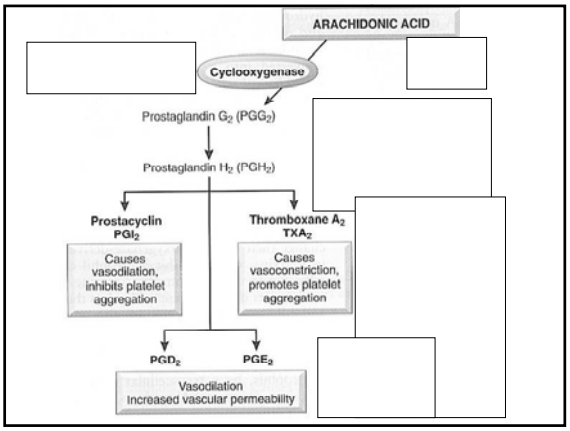
- Histamine
- Serotonin (5-OH-tryptamine)



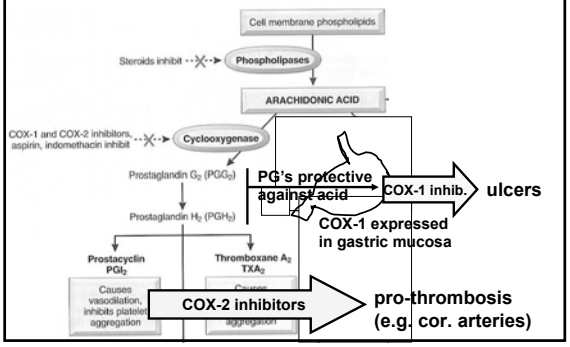


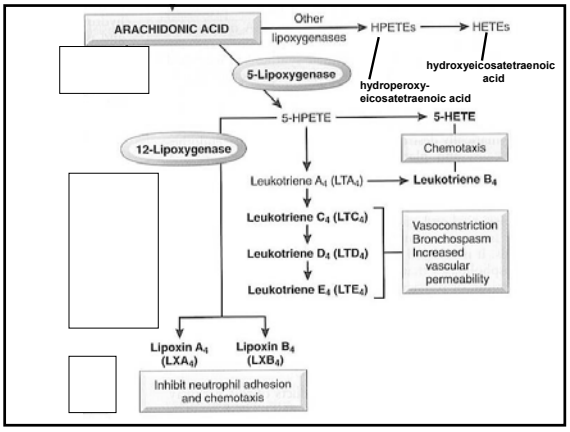
Robbins
Basic Pathology
8/e Fig. 2-15



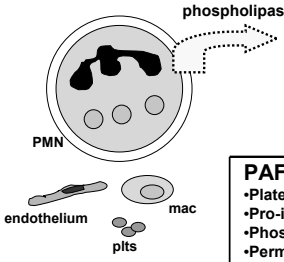


Adverse effects of anti-inflammatory drugs





Platelet Activating Factor (PAF)

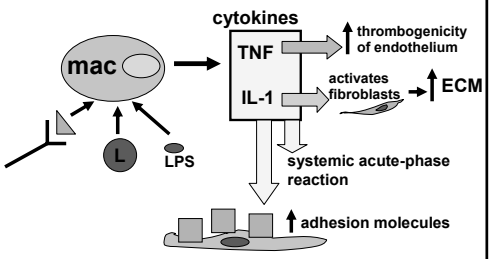


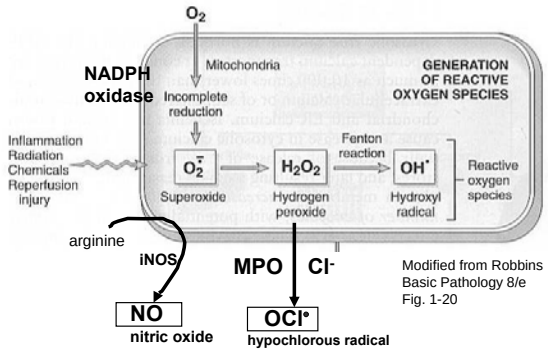
PAF
- vasodilation
- ↑ vascular permeab.
- leukocyte adhesion
- chemotaxis

PAF & the 5 P's:
- Platelet activating factor
- Pro-inflammatory
- Phospholipase A2 involved
- Permeability (↑vasc. permeab.)
- Polys (neutrophil chemotaxis)

Cytokines:

- polypeptides
- from many cells—esp. mac's and lymphocytes
- e.g. interleukins (communicate between leukocytes)

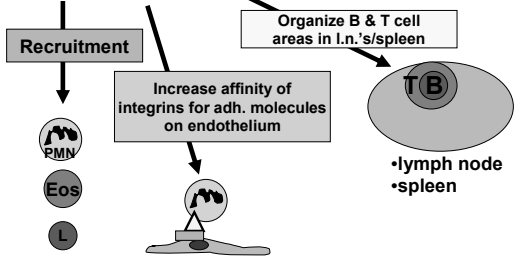


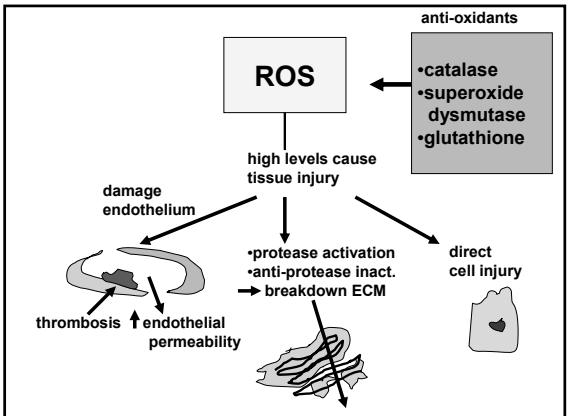


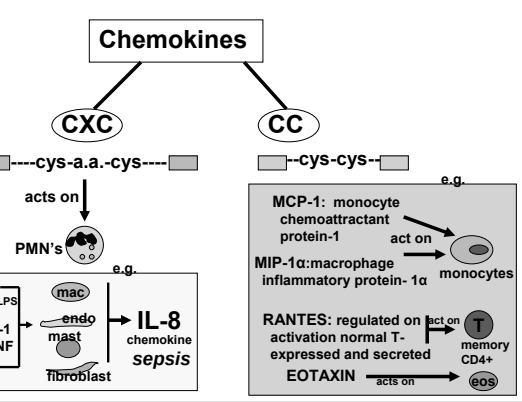
Modified from Robbins Basic Pathology 8/e Fig. 1-20

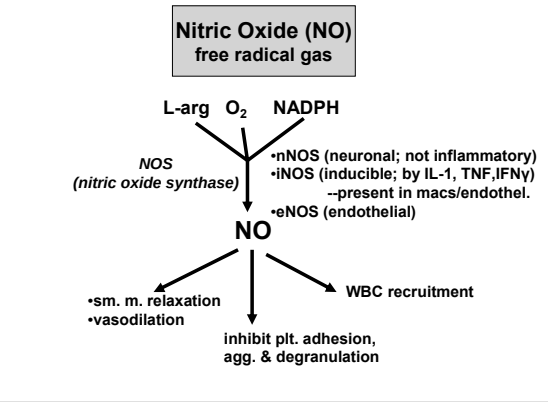
Chemokines

- Chemoattractant cytokines
- Small: 8-10 kD
- Bind to G-protein-coupled receptors on target cells

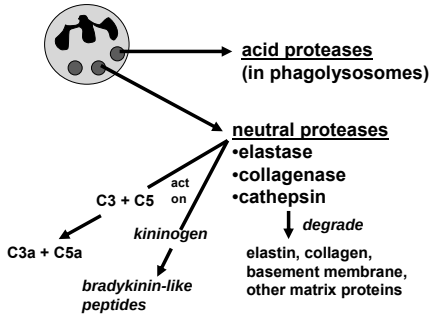








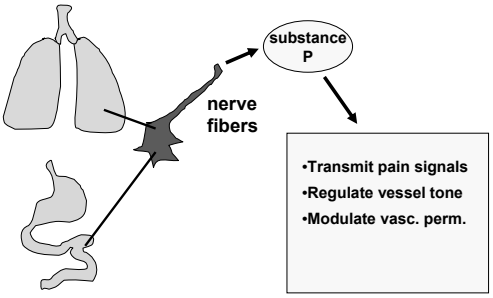
Lysosomal enzymes of leukocytes

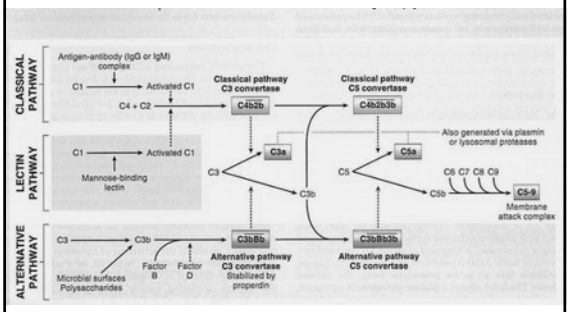


Complement

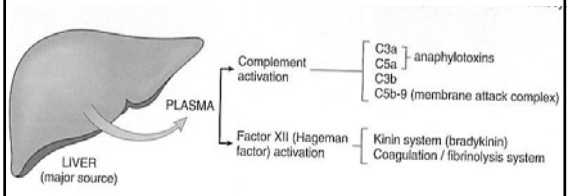
- Present in plasma as 9 inactive proteins C1 – C9
- Progressive conversions from inactive to active forms (C1→C1a, C3→C3a + C3b,etc.)
- Membrane attack complex: C5-9 forms channel in lipid membranes→ entry of fluid & ions, cell lysis
- Activation pathways:
  1. Classical (Ag-Ab complexes; IgG/IgM)
  2. Alternative (bacterial polysaccharides, e.g., endotoxin, cell wall components)
  3. Lectin (plasma mannose-binding lectin binds to mannose residues on microbes)

Neuropeptides





Plasma Protein-Derived Mediators

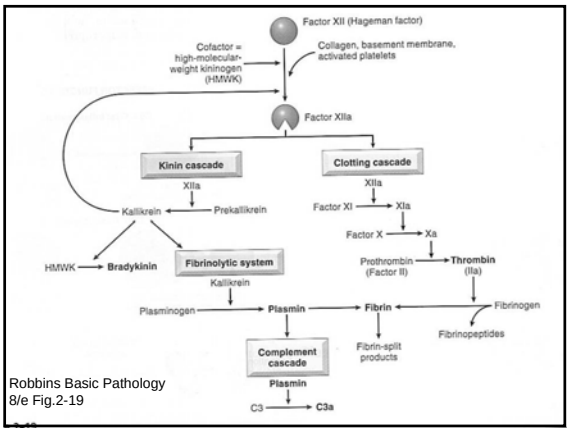


Complement roles in inflammation

Vascular
C3a + C5a
↑ vasc. permeab.
vasodilation
C3a + C5a as "anaphylatoxins"
mast cell
→ histamine

Leukocyte Chemotaxis
C5a
→ chemotaxis

Phagocytosis
C3b
iC3b (inactive)
opsonize
Bact.
C3b
iC3b



Robbins Basic Pathology
8/e Fig.2-19

Systemic Effects of Inflammation

Fever

LPS exogenous pyrogen

mac

TNF endogenous
IL-1 pyrogen

PGE_2

AA ↑ cyclo-oxyg.

hypothalamus

neurotransmitters reset temp. set point higher

↑ plasma acute-phase proteins

IL-6

C-reactive protein CRP

Serum Amyloid A SAA

fibrinogen

complement

CRP
SAA

Bact.

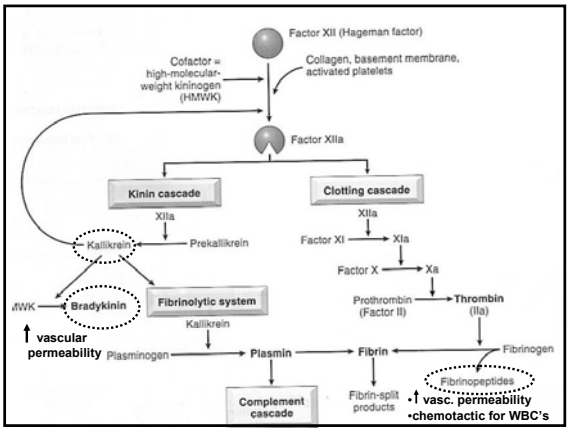
RBC rouleaux

ESR: erythrocyte Sedimentation rate

Leukocytosis

Periph. Blood WBC:
15,000-20,000 / µL
(normal 5-10,000)

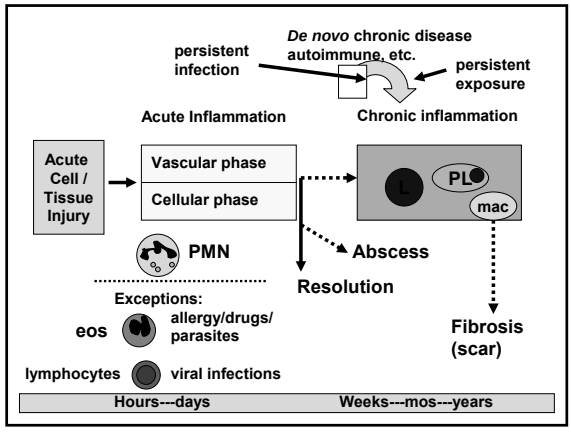
Leukemoid reaction:
40,000 – 100,000

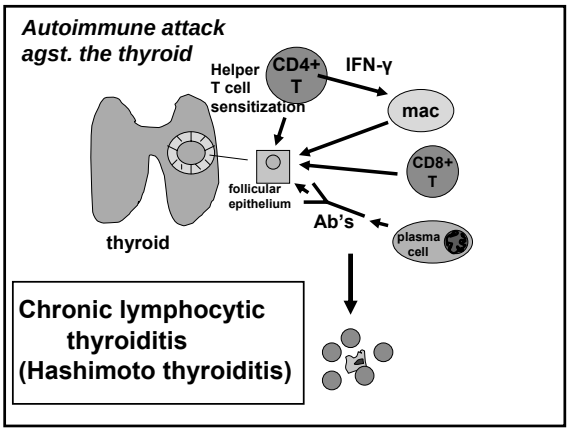


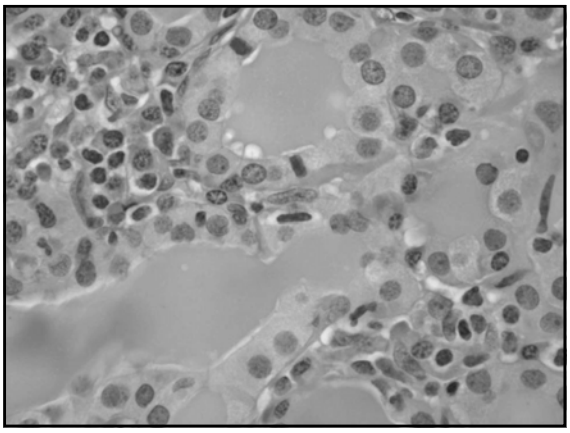
Chronic Inflammation

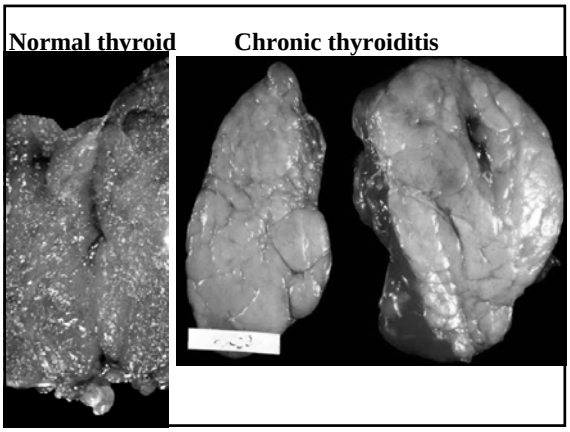
TABLE 2–6 Role of Mediators in Different Reactions of Inflammation

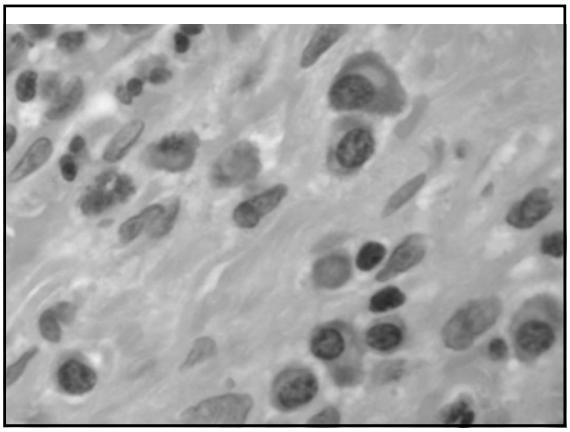
Vasodilation	Prostaglandins Nitric oxide Histamine
Increased vascular permeability	Vasoactive amines C3a and C5a (through liberating amines) Bradykinin Leukotrienes C_4, D_4, E_4 PAF Substance P
Chemotaxis, leukocyte recruitment and activation	C5a Leukotriene B_4 Chemokines IL-1, TNF Bacterial products
Fever	IL-1, TNF Prostaglandins
Pain	Prostaglandins Bradykinin
Tissue damage	Neutrophil and macrophage lysosomal enzymes Oxygen metabolites Nitric oxide

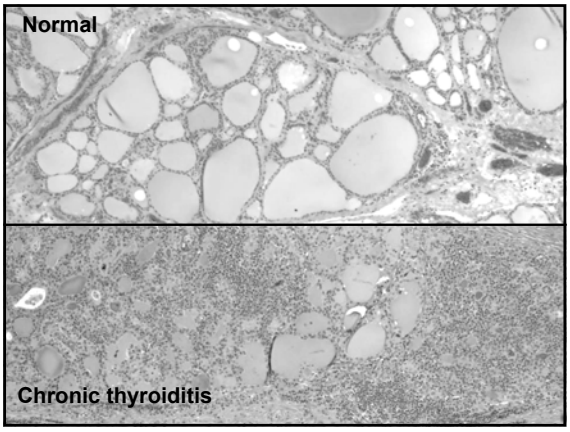


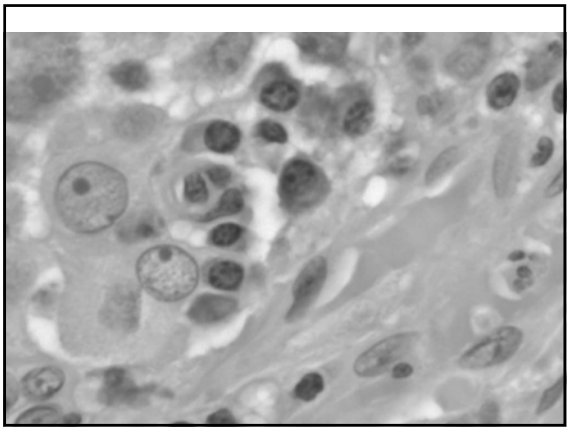

Autoimmune attack
agst. the thyroid
Helper
T cell
sensitization
CD4+
T
IFN-γ
mac
CD8+
T
follicular
epithelium
Ab's
plasma
cell
thyroid
Chronic lymphocytic
thyroiditis
(Hashimoto thyroiditis)

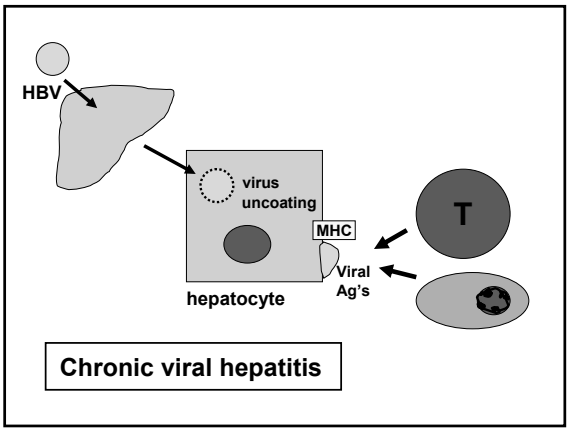



Normal thyroid
Chronic thyroiditis




Normal
Chronic thyroiditis




HBV
virus
uncoating
MHC
T
Viral
Ag's
hepatocyte
Chronic viral hepatitis