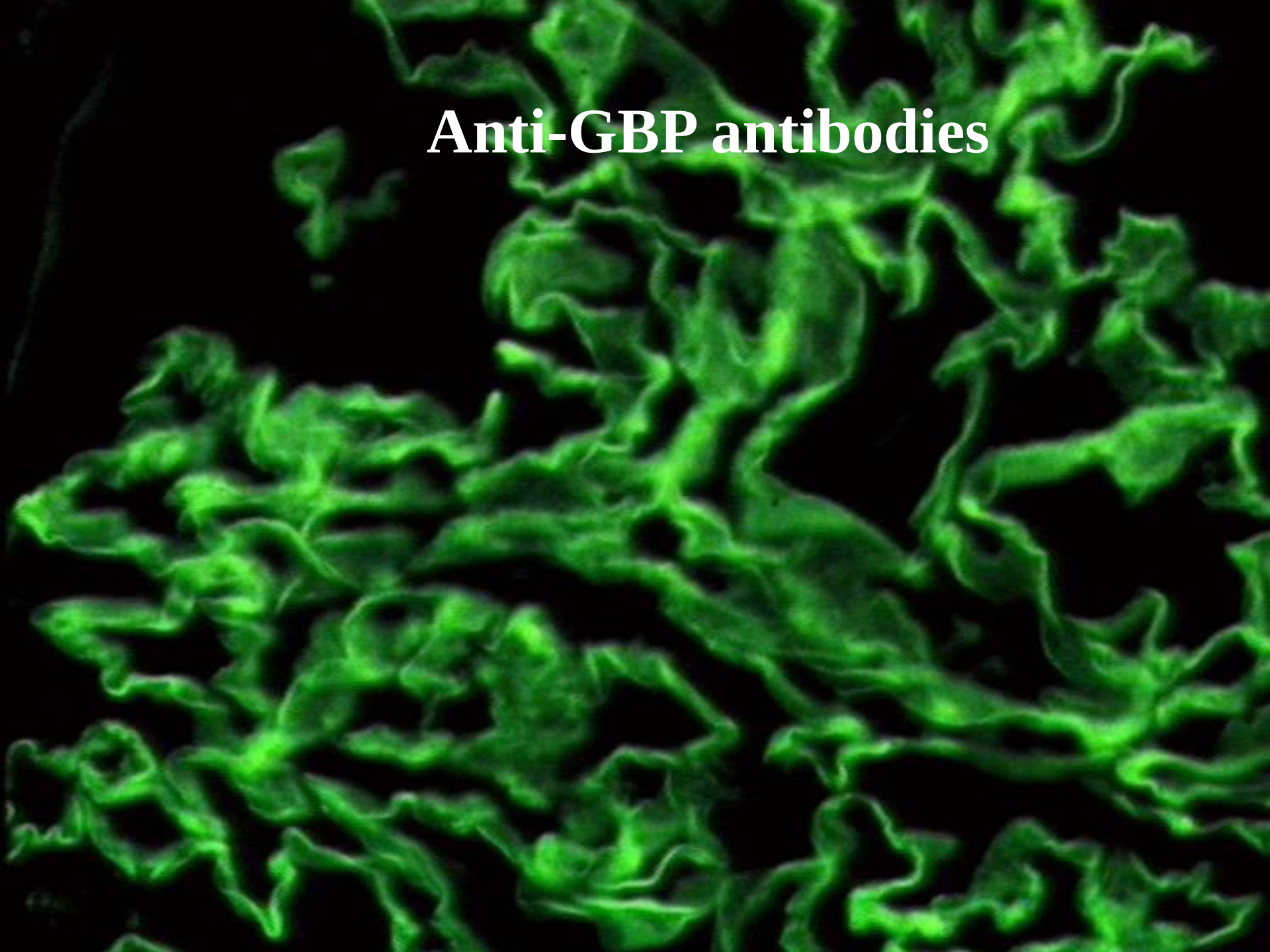
Type II-IV immunopathological reactions

Type-II hypersensitivity (cytotoxic)

- Mediated by IgG or IgM.
- Interaction between antigen and antibody leads to cell death, usually mediated by the complement system or phagocytosis.
- The antigen may be autoantigen(so it includes antibody-mediated autoimmune diseases) or may be of external origin (components of microbes, drugs.. which attach to a cell membrane).
- Includes also post-transfusion hemolytic reactions.
- Also interactions between receptors and autoantibodies (leading to receptor activation or blocade are involved in this group of hypersensitivity reactions).

Anti-GBP antibodies



Examples of antibody- mediated autoimmune diseases (type-II hypersensitivity)

Disease	Target antigen	Mechanisms of disease	Clinicopathologic manifestations
Autoimmune hemolytic anemia	Erythrocyte membrane proteins (Rh blood group antigens, I antigen)	Opsonization and phagocytosis of erythrocytes	Hemolysis, anemia
Autoimmune (idiopathic) thrombocytopenic purpura	Platelet membrane proteins (gpIIb:IIIa integrin)	Opsonization and phagocytosis of platelets	Bleeding
Pemphigus vulgaris	Proteins in intercellular junctions of epidermal cells (epidermal cadherin)	Antibody-mediated activation of proteases, disruption of intercellular adhesions	Skin vesicles (bullae)
Goodpasture's syndrome	Noncollagenous protein in basement membranes of kidney glomeruli and lung alveoli	Complement- and Fc receptor–mediated inflammation	Nephritis, lung hemorrhages
Acute rheumatic fever	Streptococcal cell wall antigen; antibody cross-reacts with myocardial antigen	Inflammation, macrophage activation	Myocarditis, arthritis
Myasthenia gravis	Acetylcholine receptor	Antibody inhibits acetycholine binding, down-modulates receptors	Muscle weakness, paralysis
Graves' disease (hyperthyroidism)	Thyroid-stimulating hormone (TSH) receptor	Antibody-mediated stimulation of TSH receptors	Hyperthyroidism
Pernicious anemia	Intrinsic factor of gastric parietal cells	Neutralization of intrinsic factor, decreased absorption of vitamin B_{12}	Abnormal erythropoiesis, anemia

Immunocomplex diseases (type III immunopathological reaction)

- Caused by deposition of immune complexes in places different from their normal metabolism.

- In case of circulating immune complexes (small, soluble complexes with excess of antigen), they deposit mainly in blood vessels walls and glomeruli leading to vasculitis and/or glomerulonephritis.
-
- Less frequent is the situation when immune complexes deposit in the place of their formation (large complexes with excess of antibodies). They deposit in the place of their formation. Extrinsic aleveolotis is the best example.

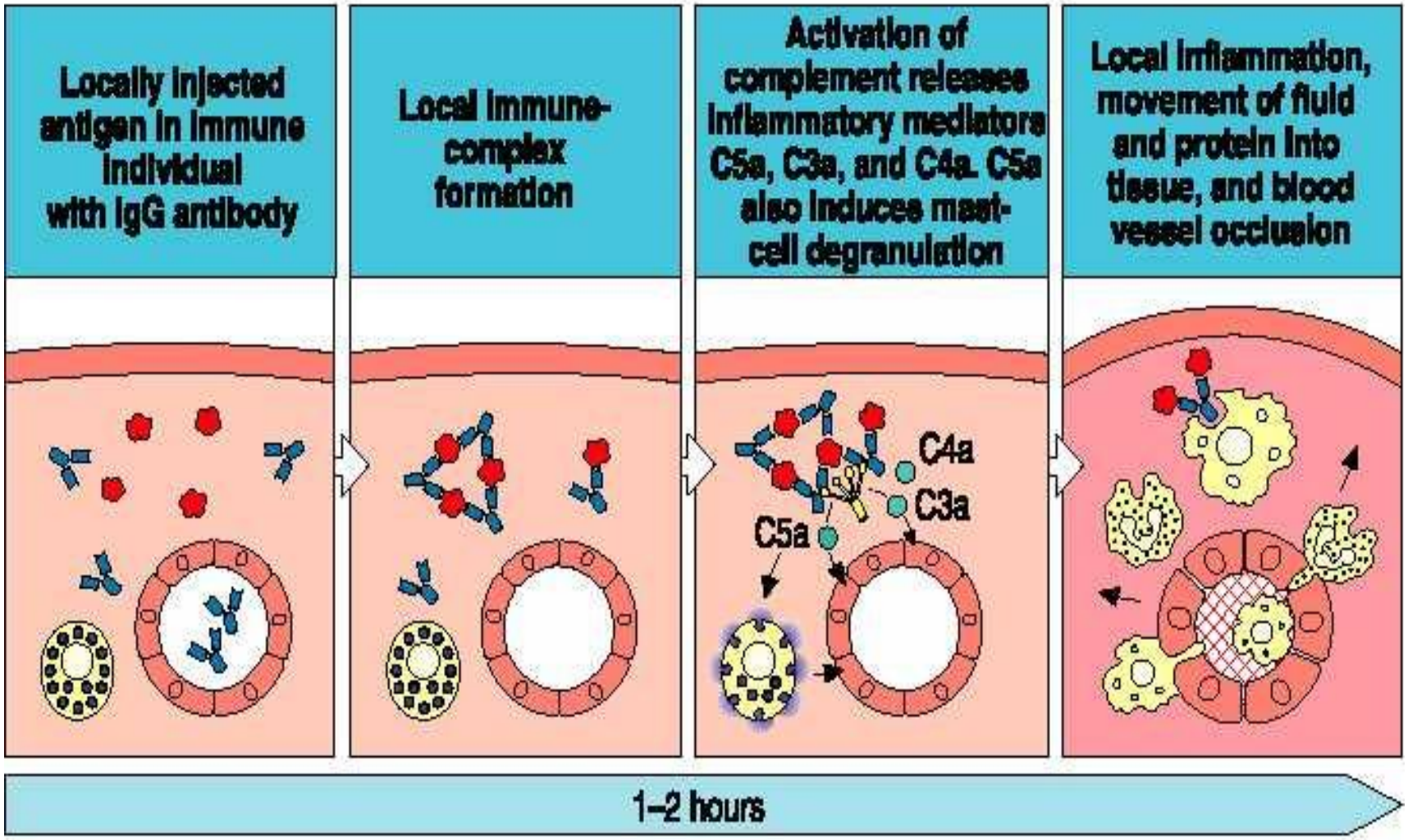
- By activation of the complement system and phagocytioc cells they induce local inflammation.

Diseases caused by immune complexes deposition – laboratory tests

- In case of deposition of immunocomplexes in vessel or glomeruli, the most important laboratory test is the direct immunofluorescence to detect the IgG part of the complexes.
- For diagnosis of extrinsic alveolitis, the presence of IgG antibodies against suspicious antigen is performed (immunodiffusion, ELISA in some instances).

Type III hypersensitivity

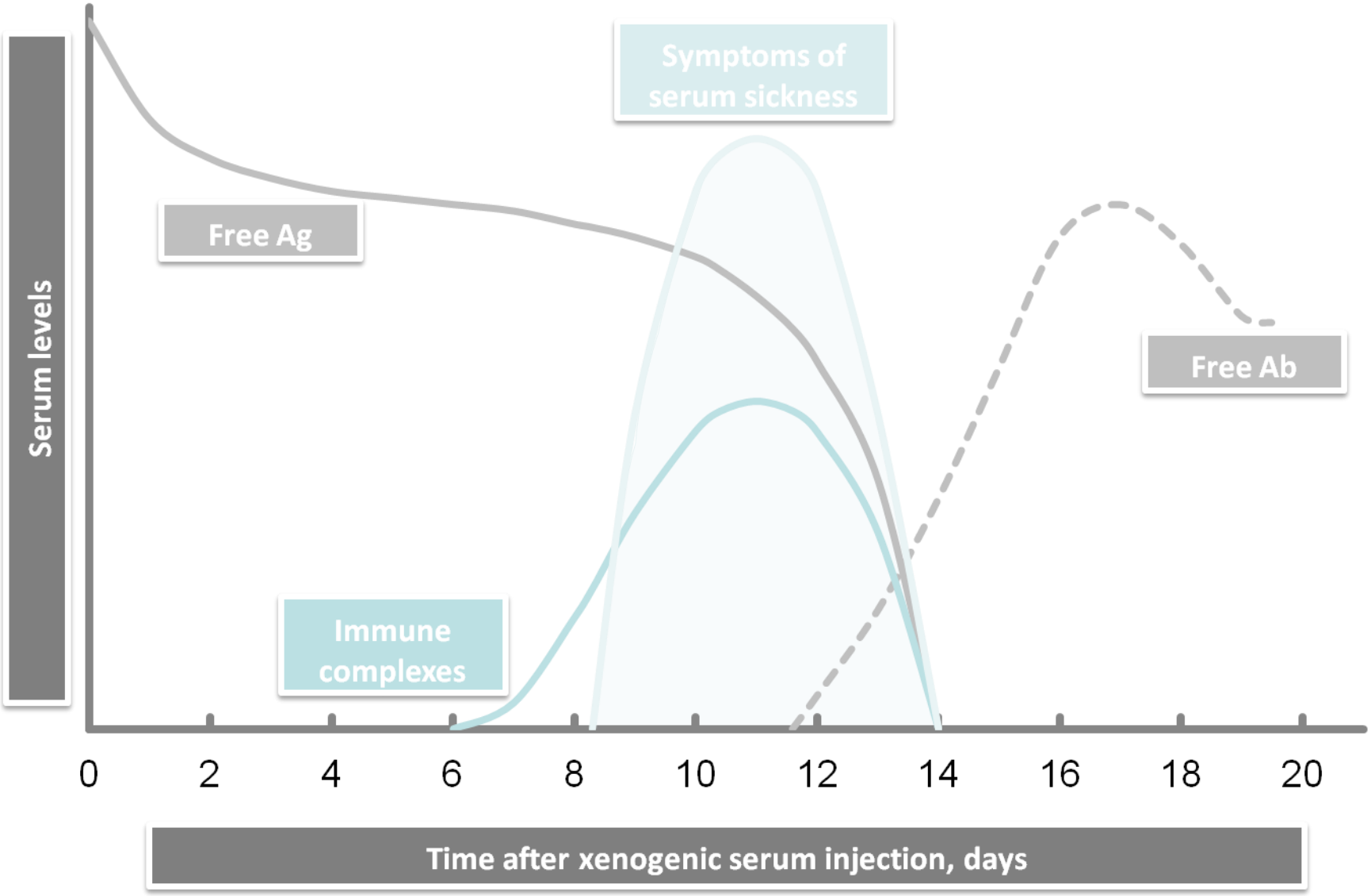
Figure 10.29



Serum sickness

- Manifests 8-12 days after use of xenogenic serum.
- Urticaria, fever, arthralgia, lymphadenopathy
- Albuminuria
- Deposits of immunocomplexes in vessels.
- Self-limiting disease, in case of need steroids or antihistaminics can be used.

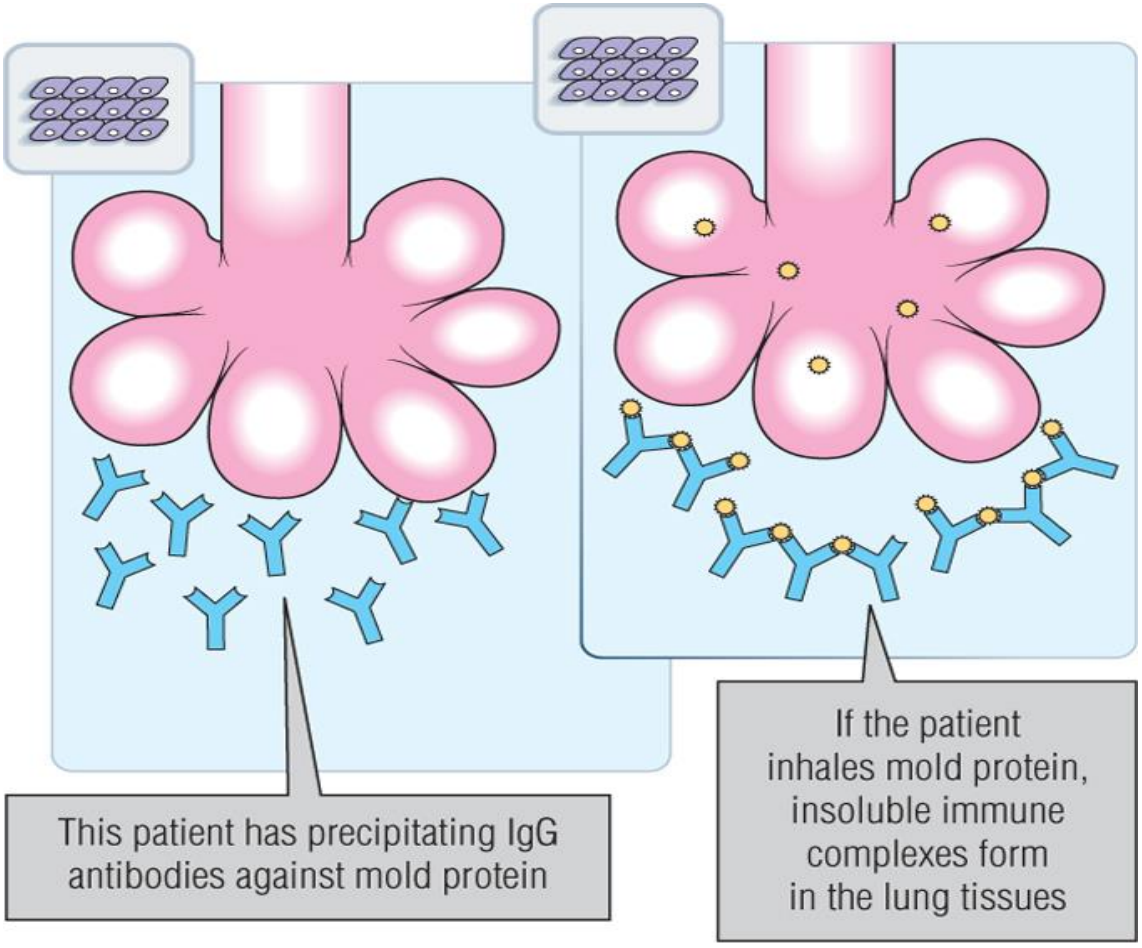
Serum Sickness



Extrinsic alveolitis

- Caused by deposition of insoluble immune complexes in the lung tissue. The complexes are formed from exogenous antigen and excess of antibodies of IgG class.
- 6-8 hours after exposition the patient suffers from dry cough, dyspnea, increased body temperature, lymphadenopathy.
- Repeated expositions lead to lung fibrosis..
- Most frequently caused by bird antigens (pigeons – pigeon breeder´s disease, parrots), thermophil actinomycetes (farmers´s lungs disease).

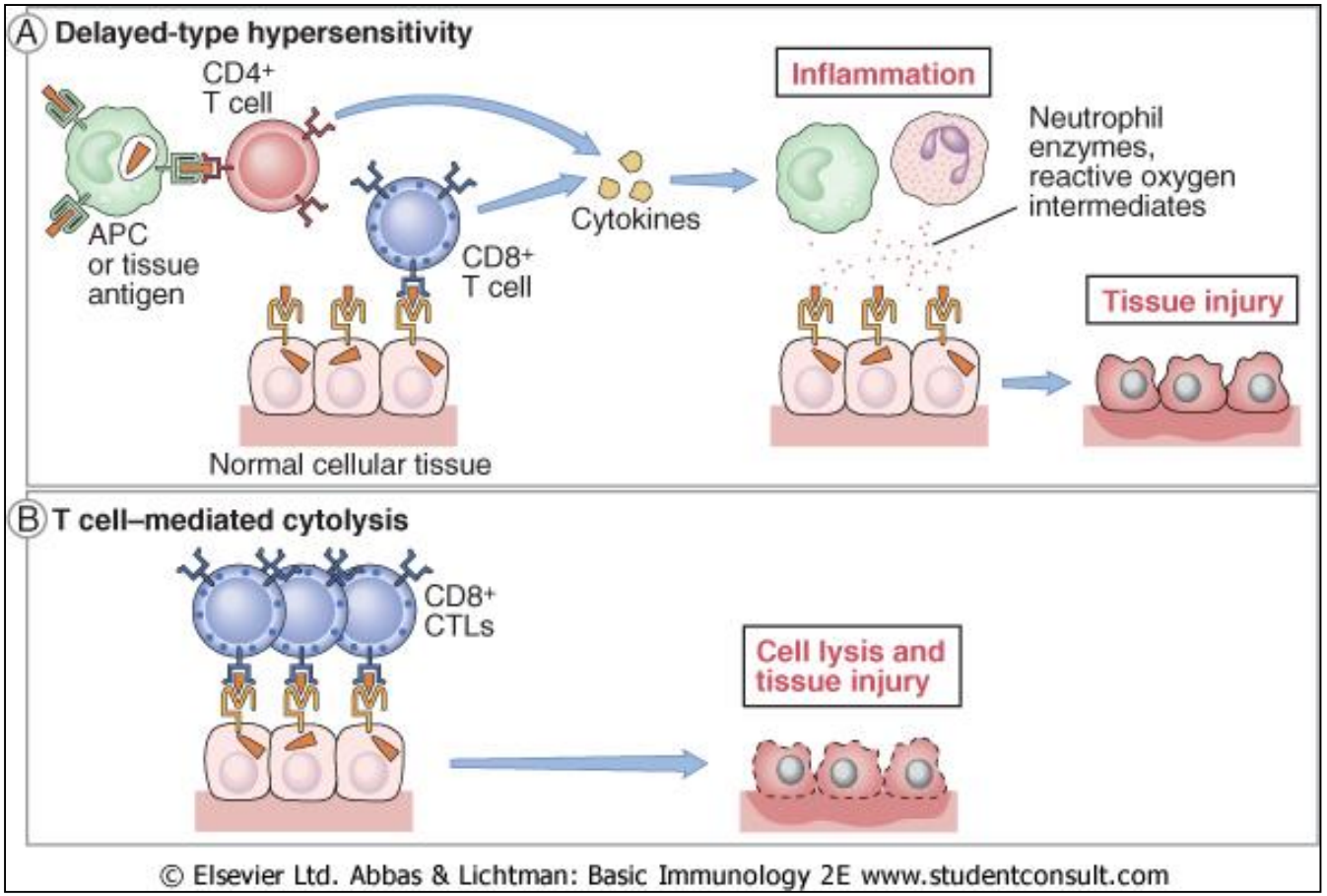
Patogenesis of extrinsic alveolitis



Type-IV hypersensitivity

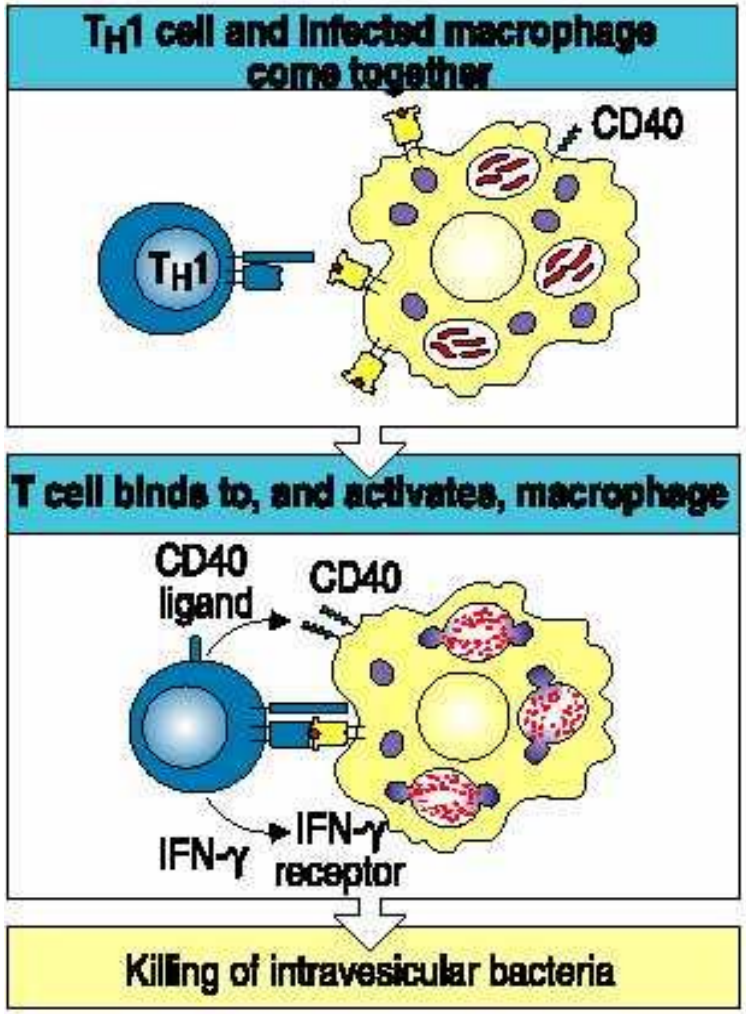
- Mediated by T-lymphocytes, predominantly Th1 lymphocytes which consequently activate macrophages – also called cellular or delayed hypersensitivity.
- This reaction develops 1-2 days after exposure – delayed type of hypersensitivity.
- Also autoimmunity caused by Tc lymphocytes is included into this group of immunopathological diseases.

Mechanisms of T-cell mediated tissue injury (type-IV hypersensitivity)

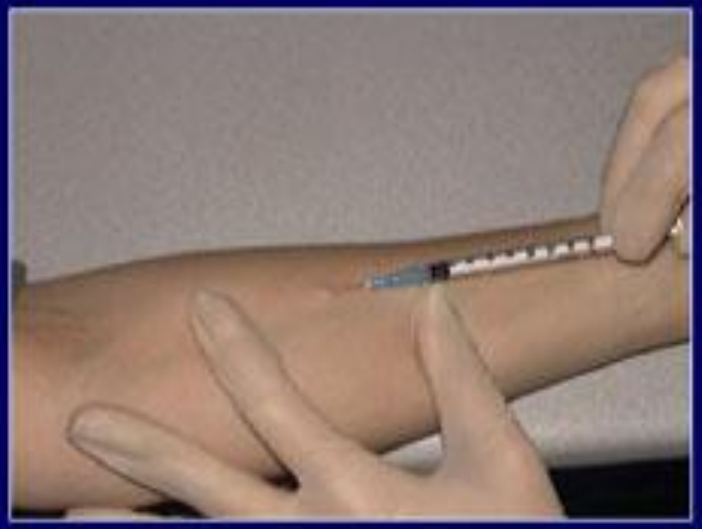


Function of Th1 cells

Figure 6.27



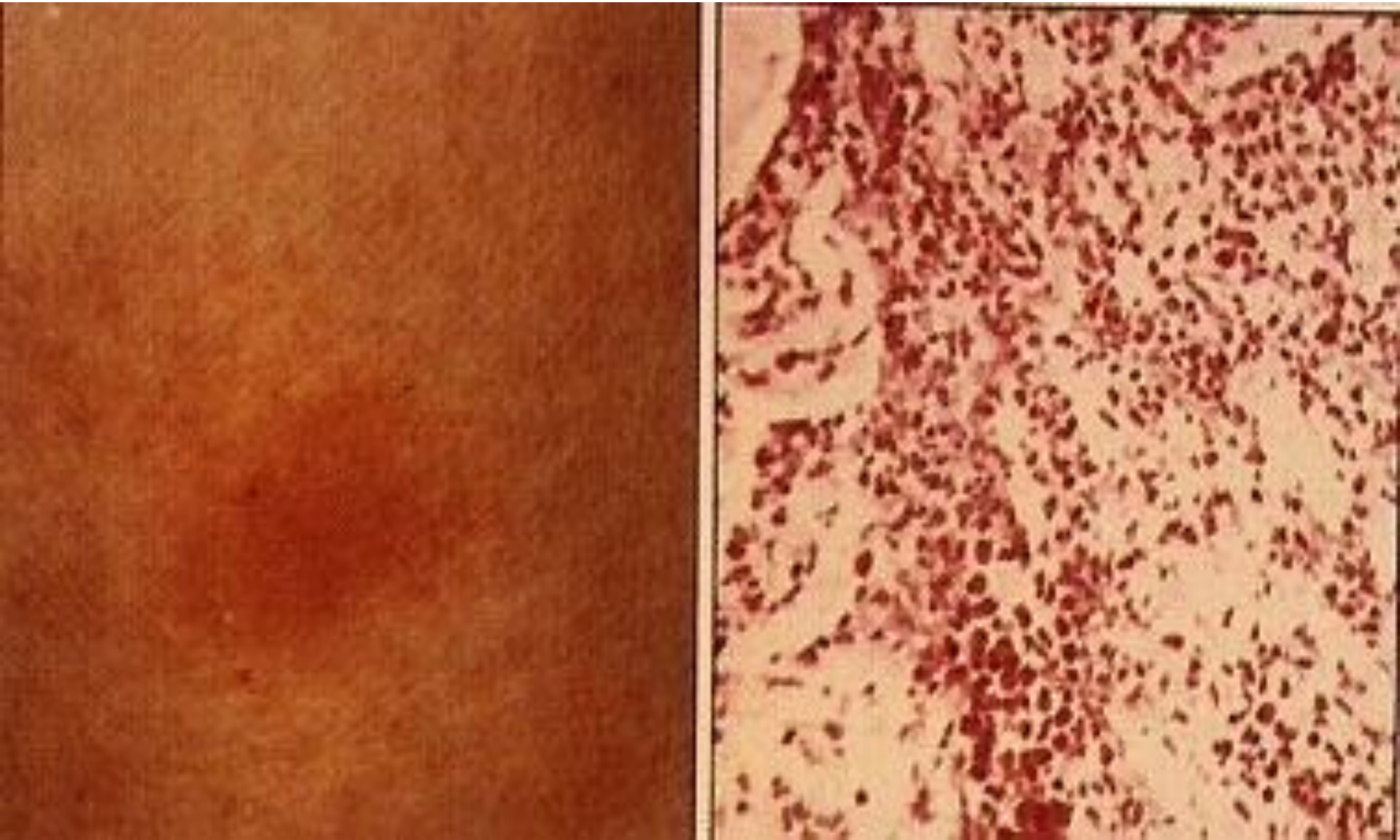
Administering the Tuberculin Skin Test



- Inject intradermally 0.1 ml of 5 TU PPD tuberculin
- Produce wheal 6 mm to 10 mm in diameter
- Do not recap, bend, or break needles, or remove needles from syringes
- Follow universal precautions for infection control

CDC

Tuberculin reaction



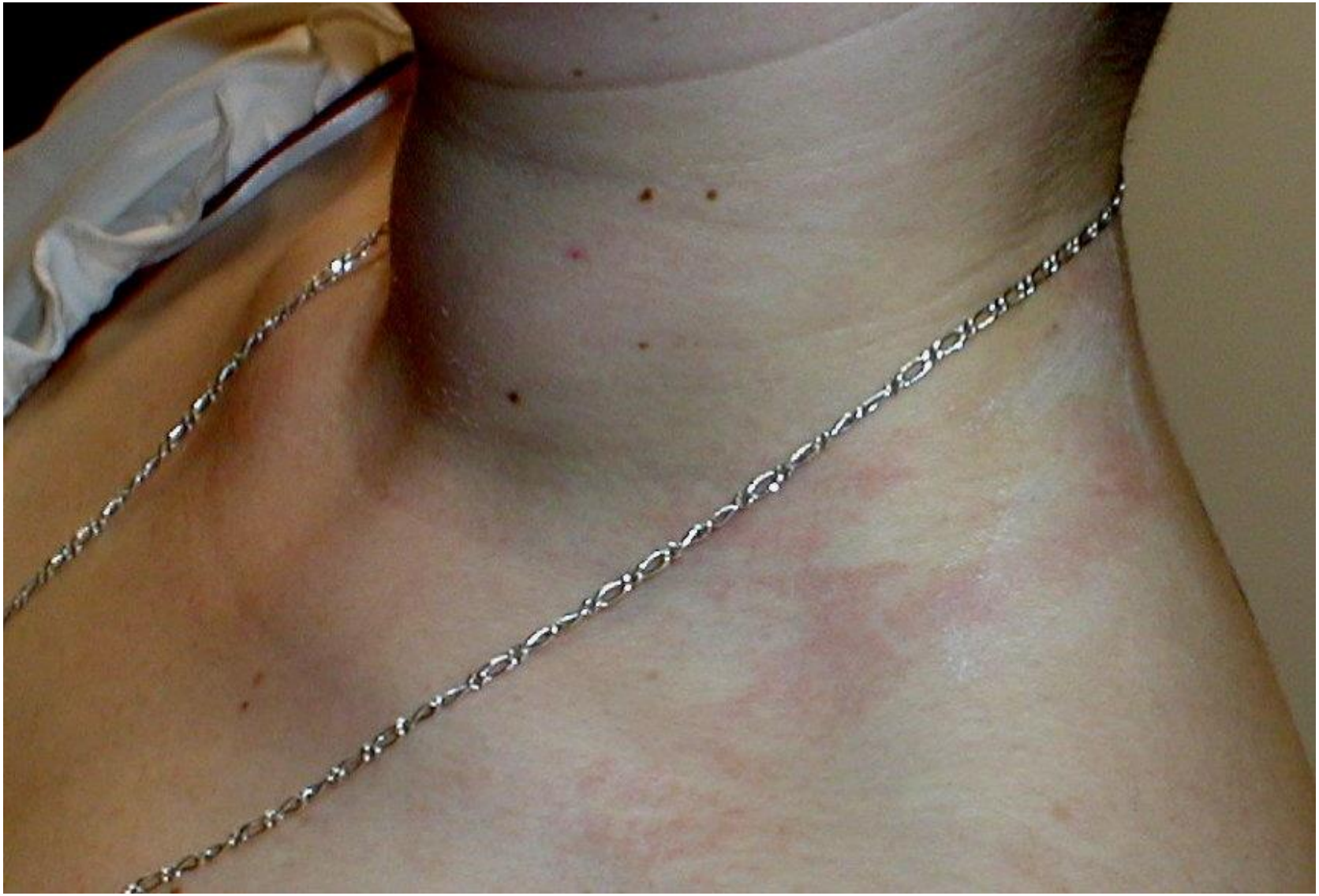
Examples of diseases where type-IV hypersensitivity plays a key role

- Contact exzema
- Cavitation in tuberculosis
- Sarcoidosis
- Several types of vasculitis
- Autoimmune diseases where T-lymphocytes play a major role (multiple sclerosis)

Contact eczema (contact dermatitis)

- Contact dermatitis is a red, itchy rash caused by direct contact with a substance as a type-IV allergic reaction to it.
- The reaction develops several days after the exposure.
- Many substances can cause such reactions, including soaps, cosmetics, perfumes, metals (incl. jewelry), plants.

Contact dermatitis due to nickel hypersensitivity



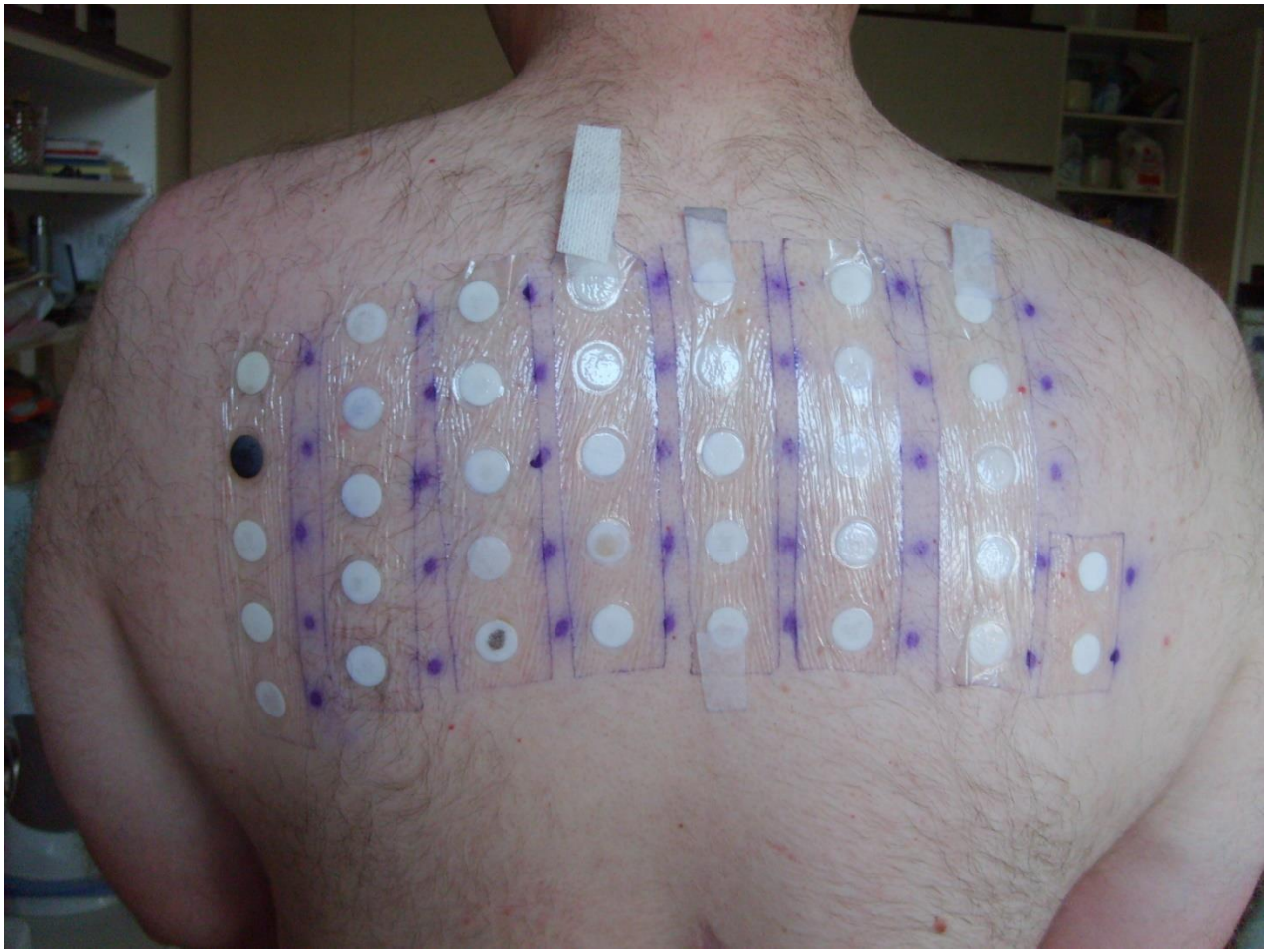
Allergy Capital: *Contact dermatitis*. Australian Allergy, Asthma and Immunology Information.
http://www.allergycapital.com.au/allergycapital/Contact_dermatitis.html

Contact dermatitis

Skin patch test

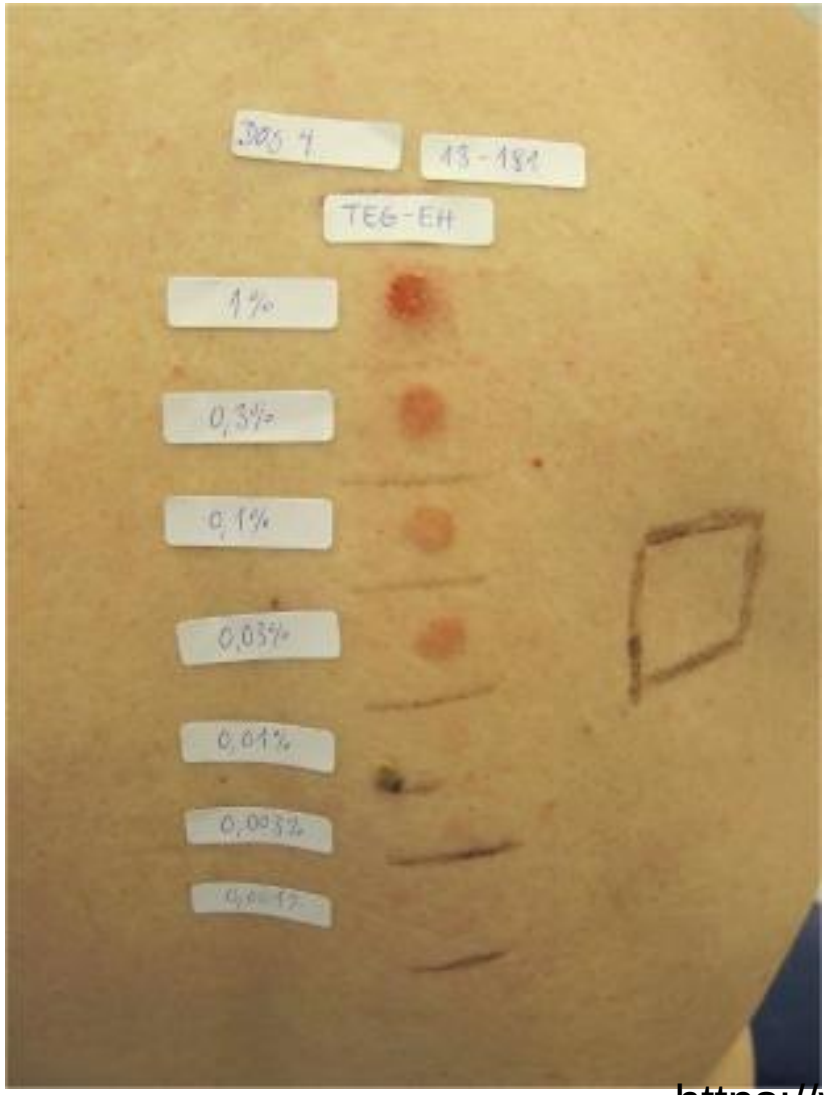
- Is used for detection of type-IV hypersensitivity (usually in the case of contact eczema).
- The antigen is included into an ointment.
- The ointment with the antigen is placed on the skin and covered by an adhesive tape.
- After one day, the tape + the antigen are washed.
- The results are read the next day.
- A positive reaction is an eczema-like exanthema (red skin spots).

Patch tests



Wikipedia

Patch tests - results



https://www.researchgate.net/