Hipersibilidade tipo IV

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Hipersensibilidade do tipo IV ou Tardia (DTH)

- ✓Reações Mediadas por Células

Tipos de Hipersensibilidade

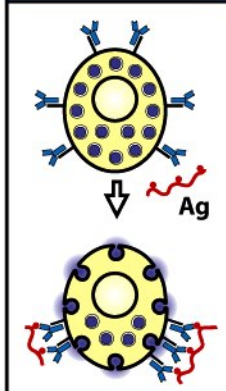
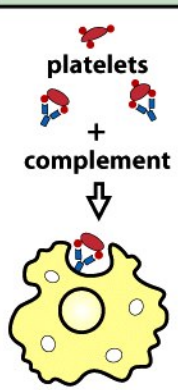
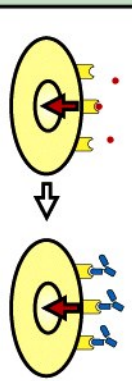
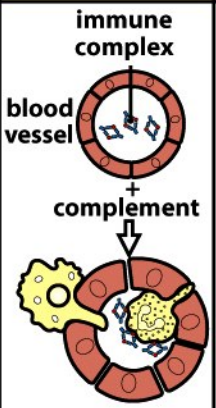
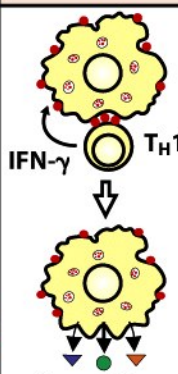
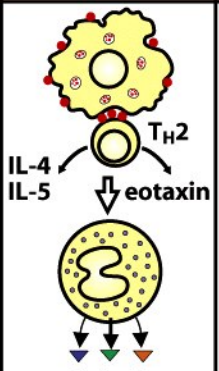
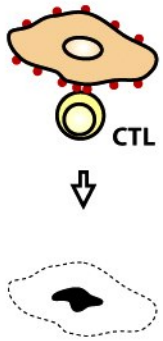
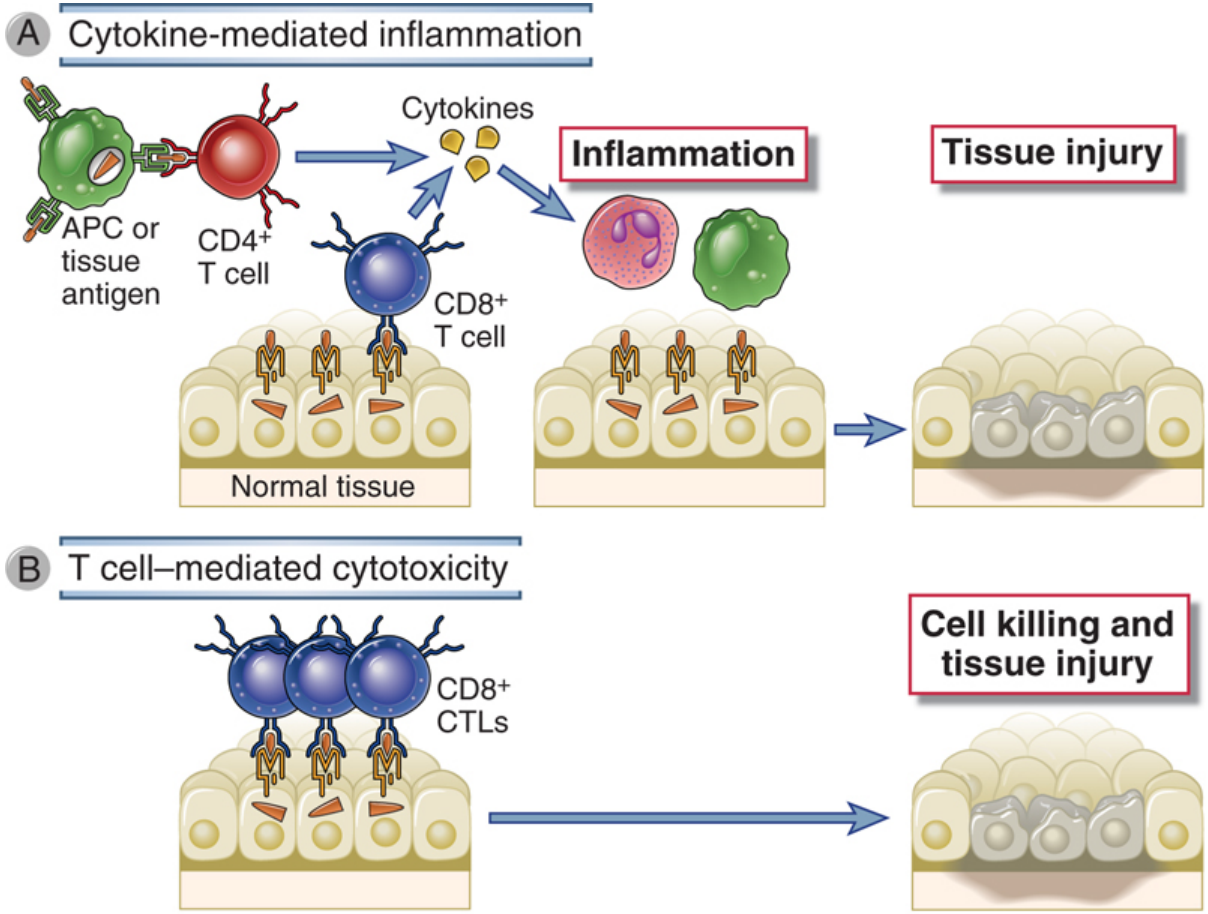
	Type I	Type II		Type III	Type IV		
Immune reactant	IgE	IgG		IgG	T_H1 cells	T_H2 cells	CTL
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Cell-surface receptor	Soluble antigen	Soluble antigen	Soluble antigen	Cell-associated antigen
Effector mechanism	Mast-cell activation	Complement, FcR^+ cells (phagocytes, NK cells)	Antibody alters signaling	Complement, phagocytes	Macrophage activation	IgE production, eosinophil activation, mastocytosis	Cytotoxicity
							
Example of hypersensitivity reaction	Allergic rhinitis, asthma, systemic anaphylaxis	Some drug allergies (e.g. penicillin)	Chronic urticaria (antibody against FCεRIα)	Serum sickness, Arthus reaction	Contact dermatitis, tuberculin reaction	Chronic asthma, chronic allergic rhinitis	Graft rejection

Figure 13-1 Immunobiology, 7ed. (© Garland Science 2008)

Lesão induzida por Células

- Lesão tecidual local
- Células T
- Após horas do contato com o antígeno



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Tipos de Hipersensibilidades do Tipo IV

Type IV hypersensitivity reactions are mediated by antigen-specific effector T cells		
Syndrome	**Antigen**	**Consequence**
Delayed-type hypersensitivity	**Proteins:** **Insect venom** **Mycobacterial proteins (tuberculin, lepromin)**	**Local skin swelling:** **Erythema** **Induration** **Cellular infiltrate** **Dermatitis**
Contact hypersensitivity	**Haptens:** **Pentadecacatechol (poison ivy)** **DNFB** **Small metal ions:** **Nickel** **Chromate**	**Local epidermal reaction:** **Erythema** **Cellular infiltrate** **Vesicles** **Intraepidermal abscesses**
Gluten-sensitive enteropathy (celiac disease)	**Gliadin**	**Villous atrophy in small bowel** **Malabsorption**

Figure 13-28 Immunobiology, 7ed. (© Garland Science 2008)

Reação de Hipersensibilidade do tipo Tardia (DTH)

- *Teste: reação tuberculínica*

Derivado protéico purificado (PPD) do *Mycobacterium tuberculosis*

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Reação de DTH

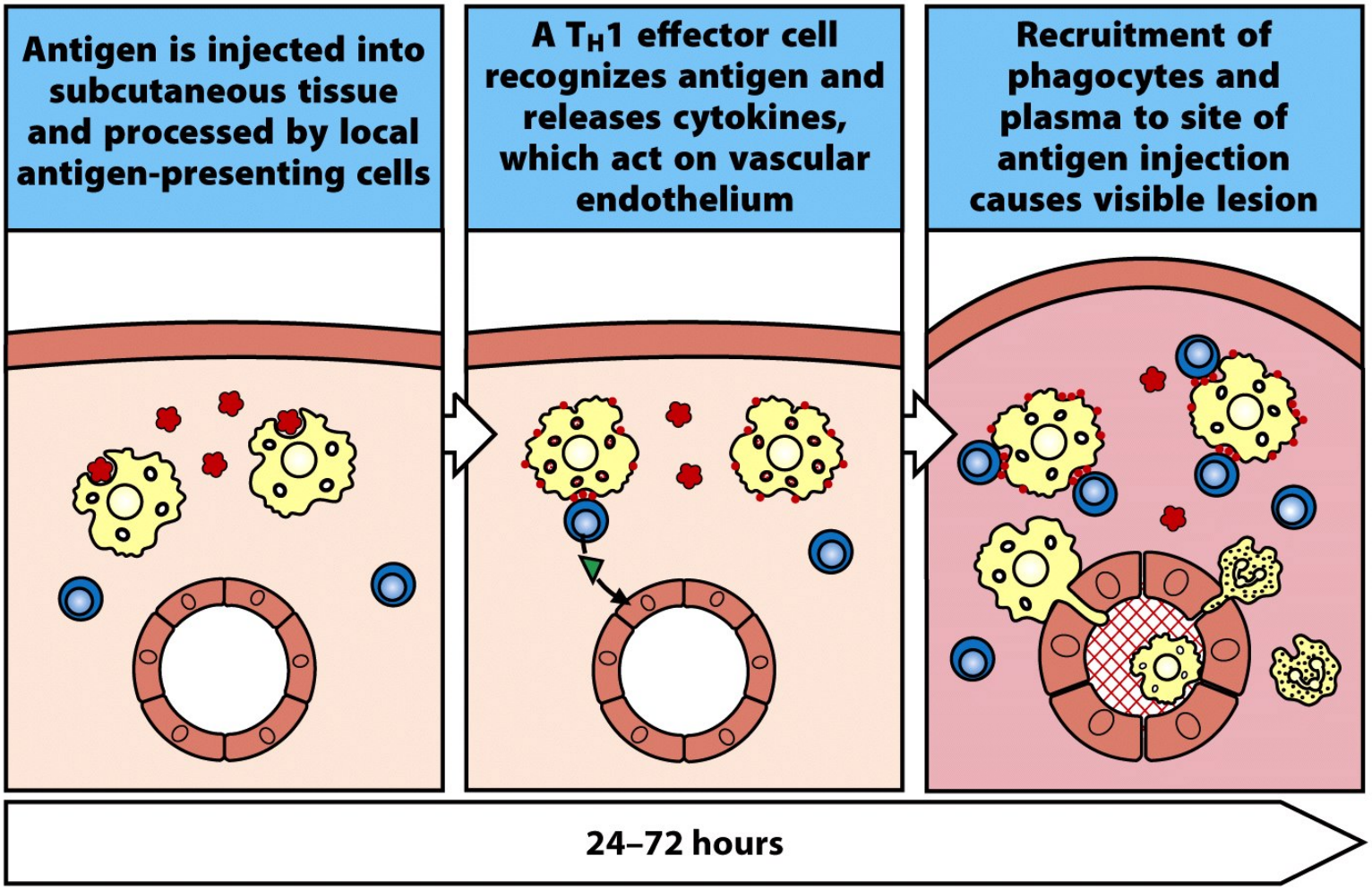


Figure 13-29 Immunobiology, 7ed. (© Garland Science 2008)

DTH é mediada principalmente por linfócitos Th1

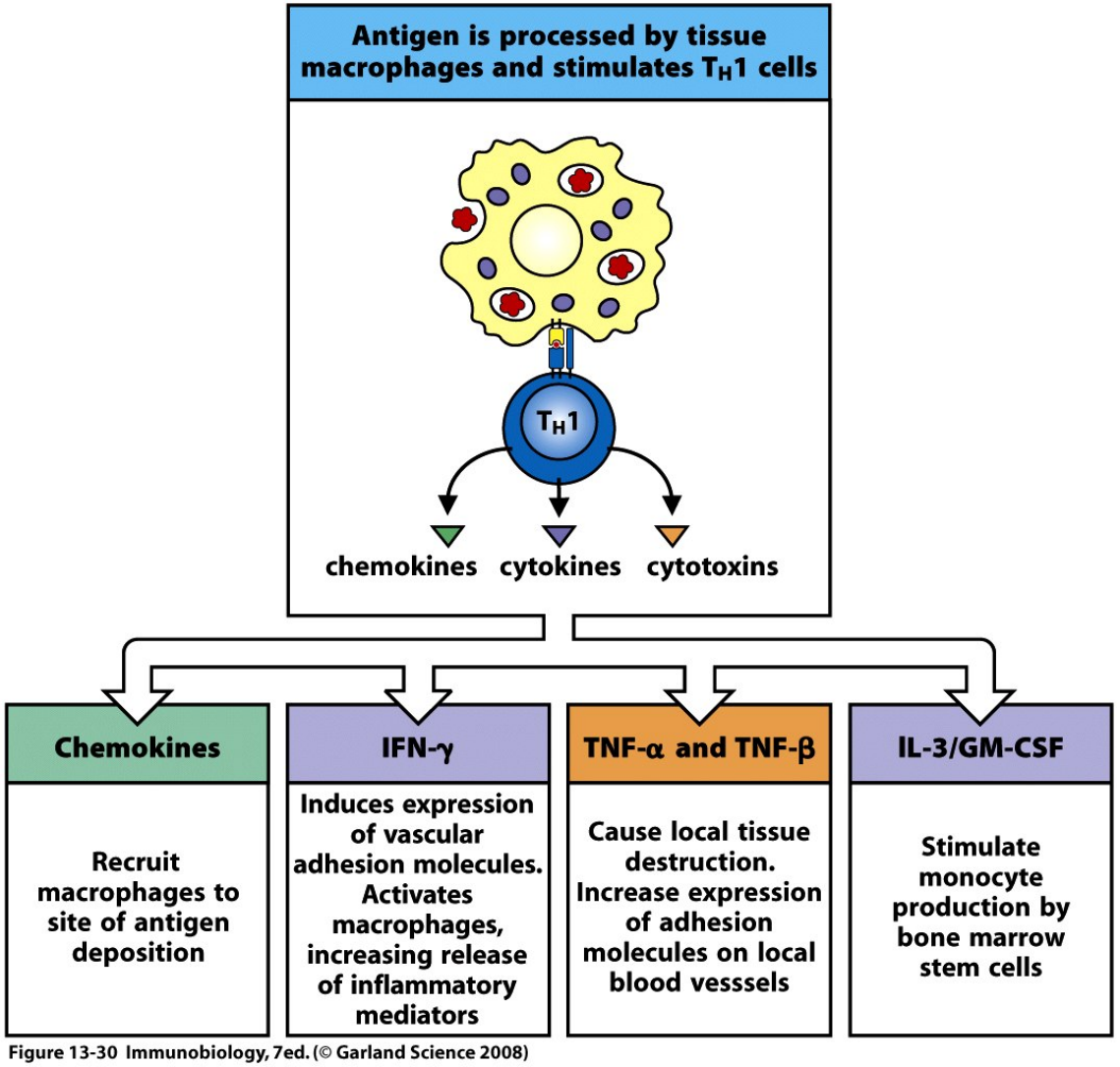
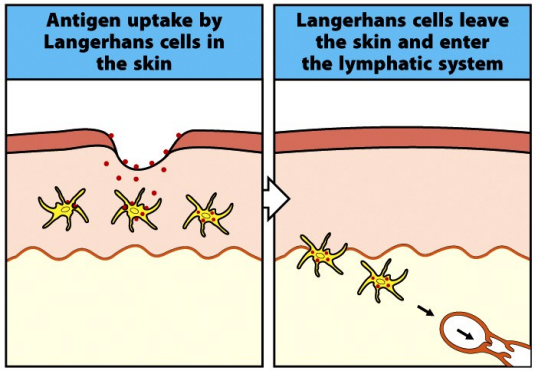


Figure 13-30 Immunobiology, 7ed. (© Garland Science 2008)

Fases da Hipersensibilidade tipo IV



1- Fase de sensibilização

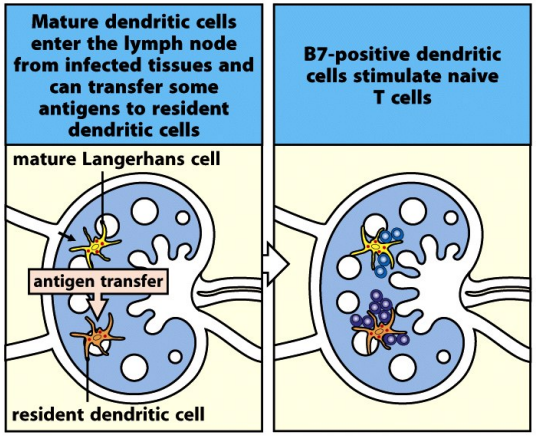


Figure 8-13 Immunobiology, 7ed. (© Garland Science 2008)

2-Fase de Reação (Elicitação)

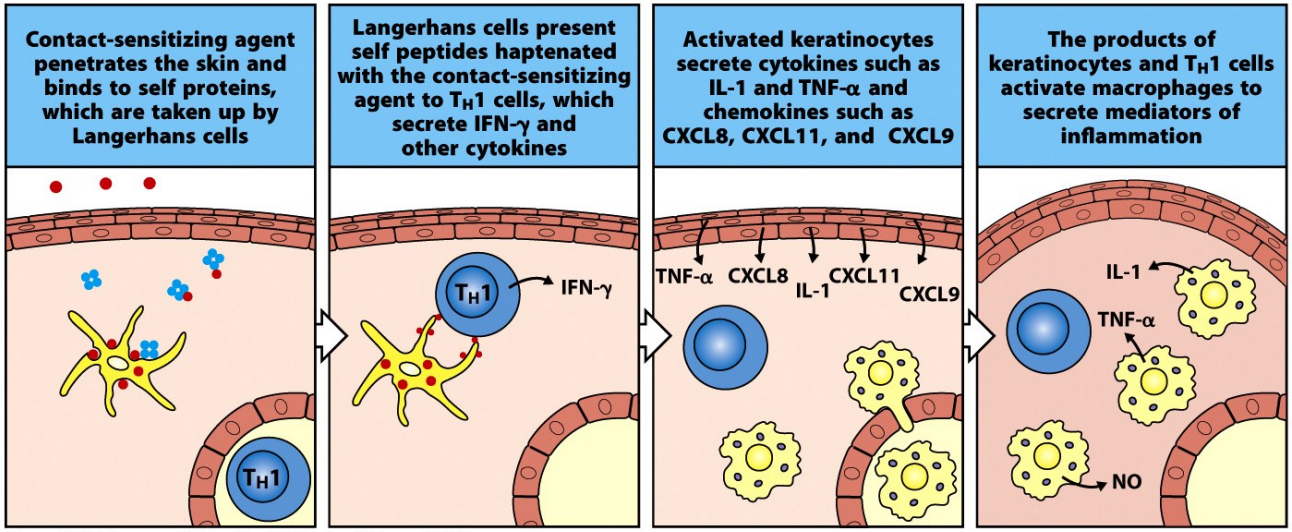
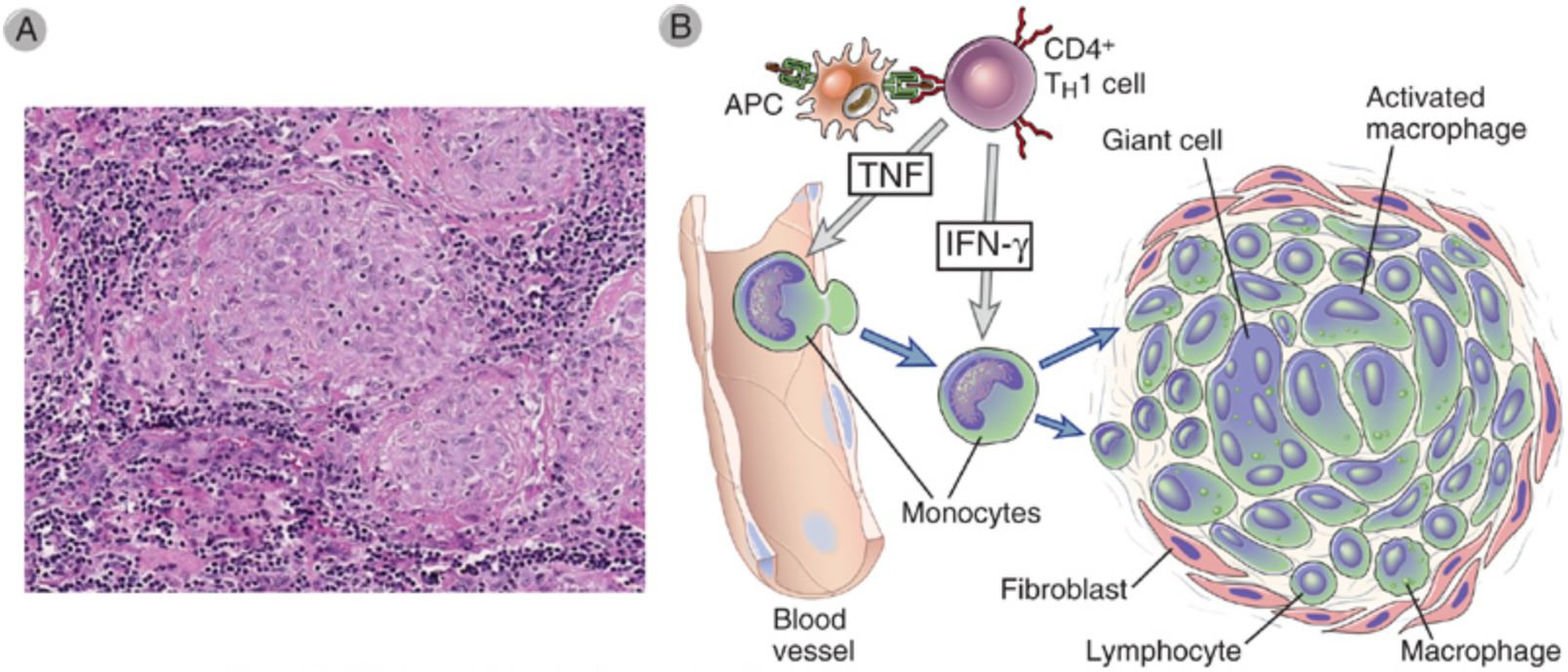


Figure 13-31 Immunobiology, 7ed. (© Garland Science 2008)

Formação de Granuloma



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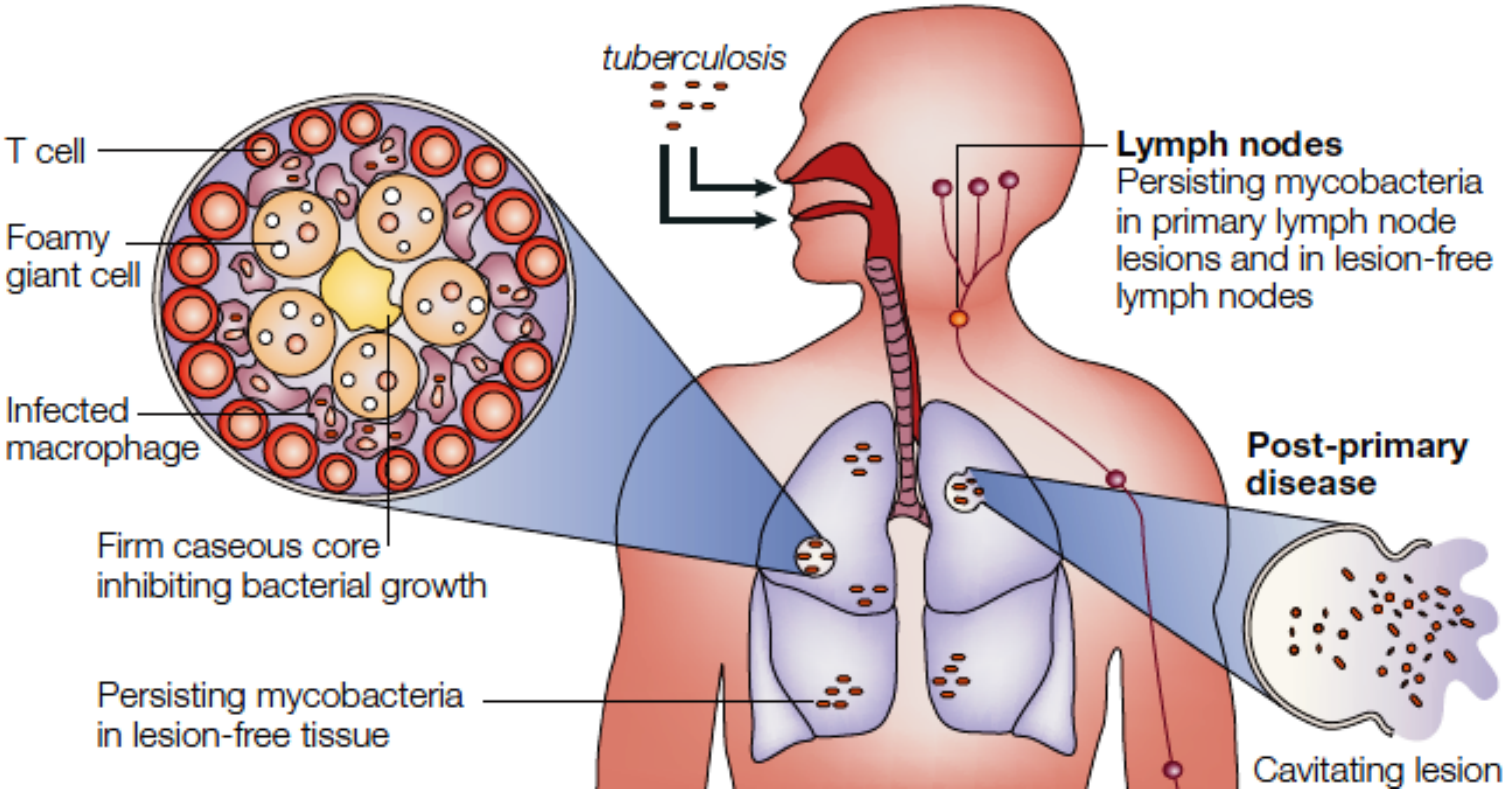
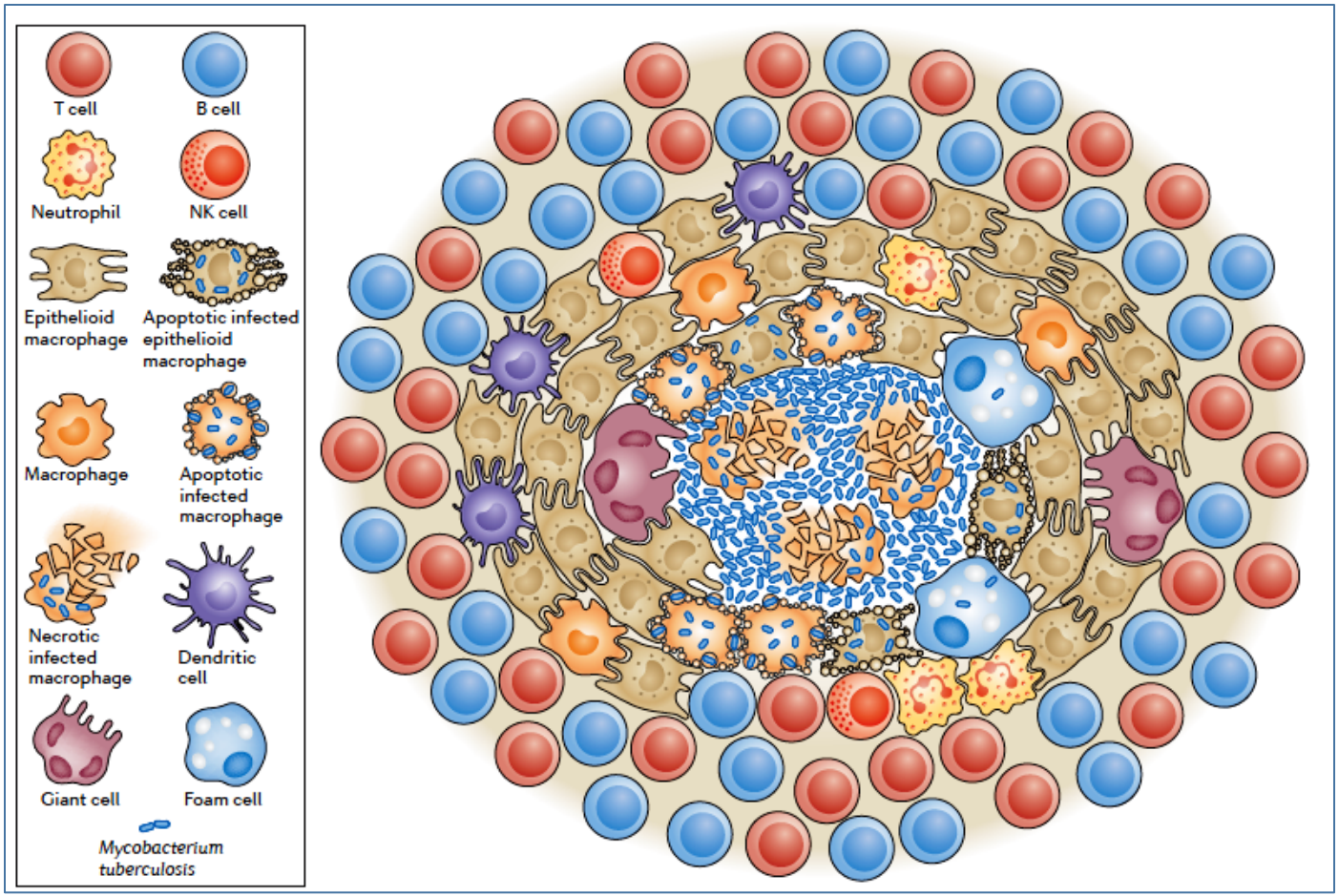
Tuberculose
Mycobacterium tuberculosis

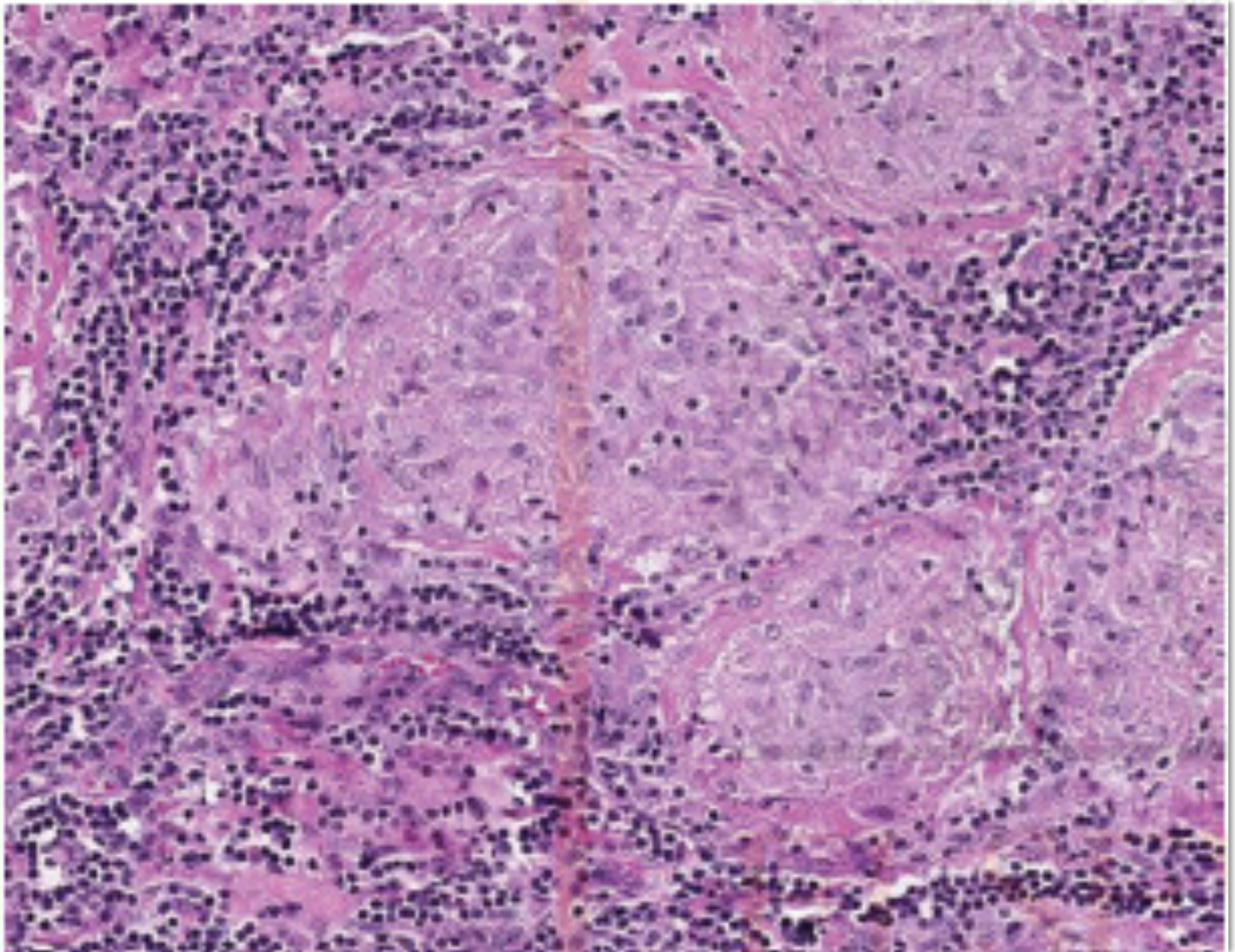
- Tuberculose – *Mycobacterium tuberculosis*



Hipersensibilidade do tipo tardia - DTH

- *Fibrose do tecido pulmonar → dificuldade respiratória*





Hipersensibilidade de Contato

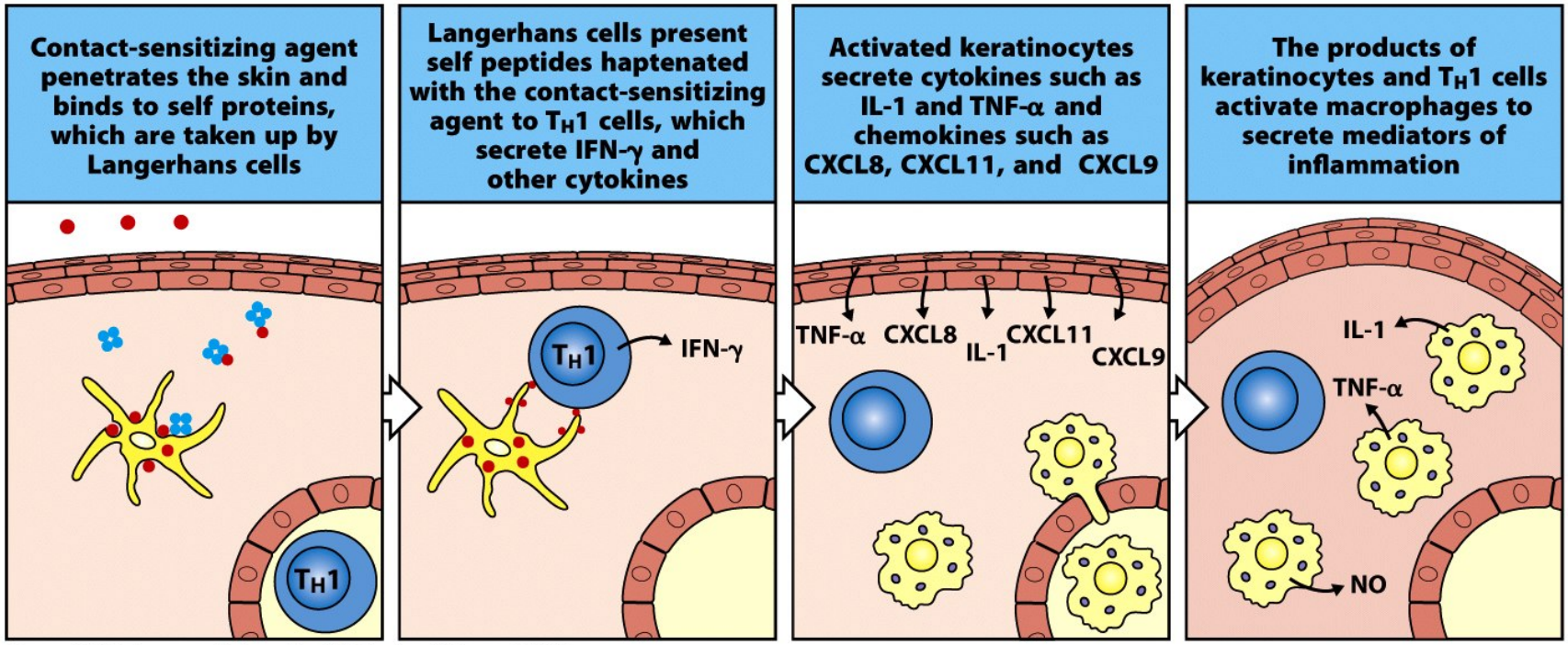


Figure 13-31 Immunobiology, 7ed. (© Garland Science 2008)

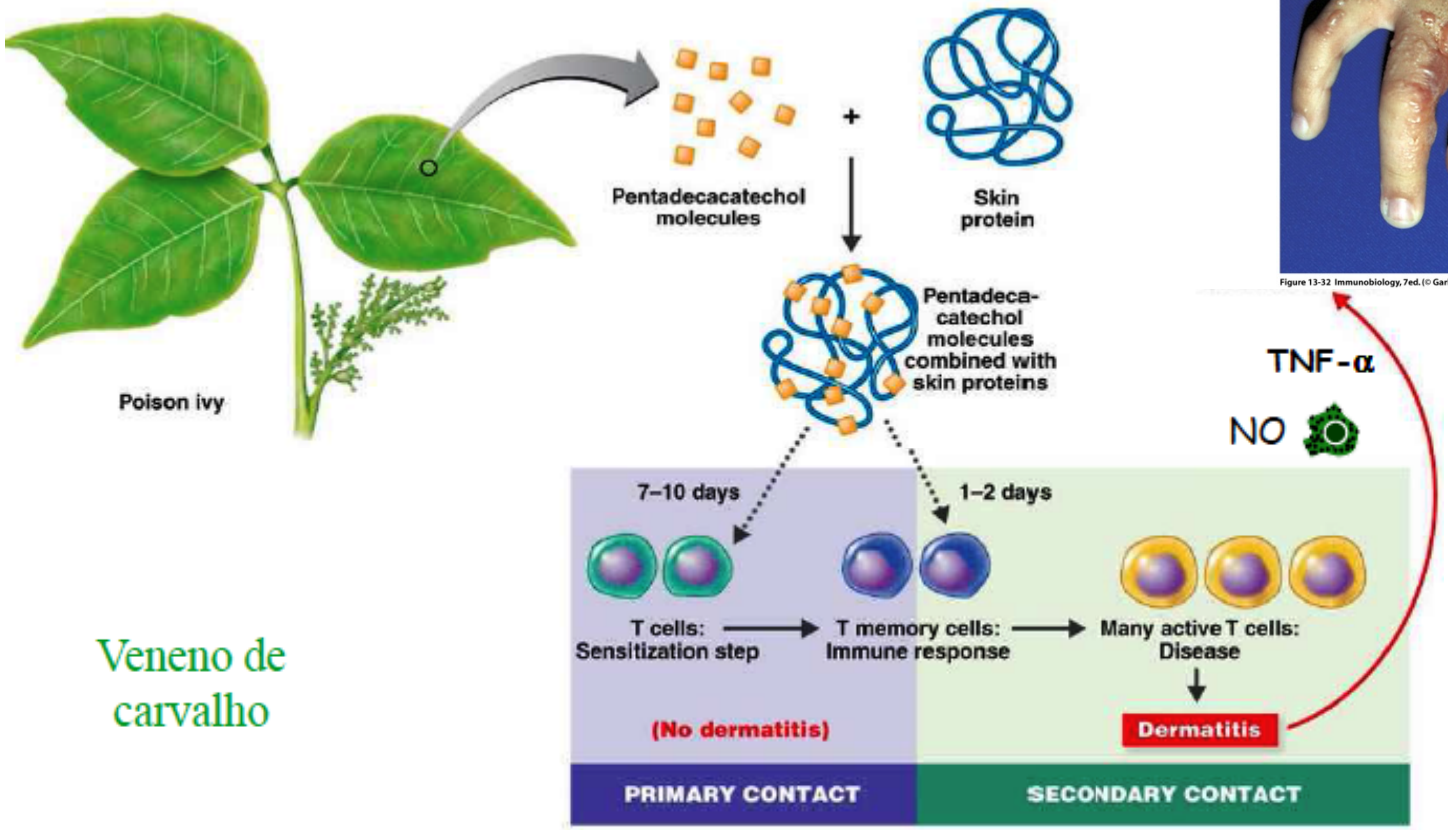
Dermatite de Contato por Hera Venenosa

Figure 13-32 Immunobiology, 7ed. (© Garland Science 2008)

Dermatite de Contato por Hera Venenosa

Hera venenosa: pentadecacatecol (hapteno)

Células TCD8^{+}



Veneno de carvalho

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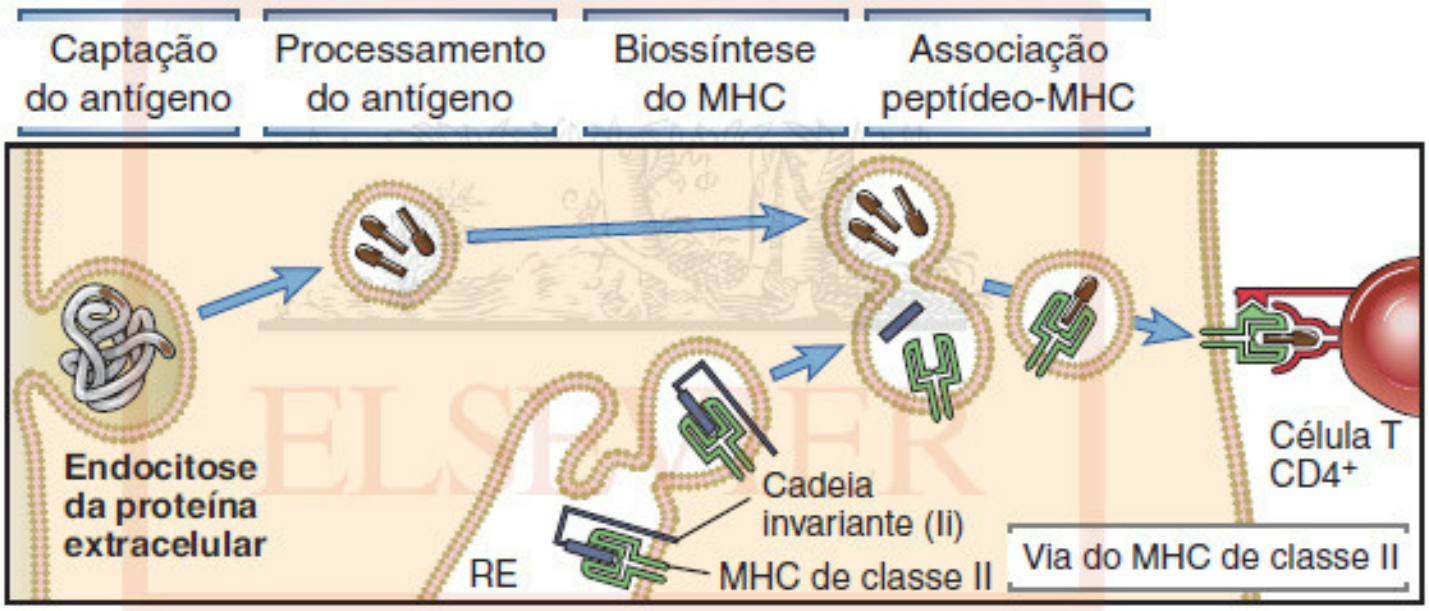
Hipersensibilidade de Contato

Cloreto pícrico: corante

- ✓ Modifica proteínas próprias extracelulares
- ✓ Células TCD4+



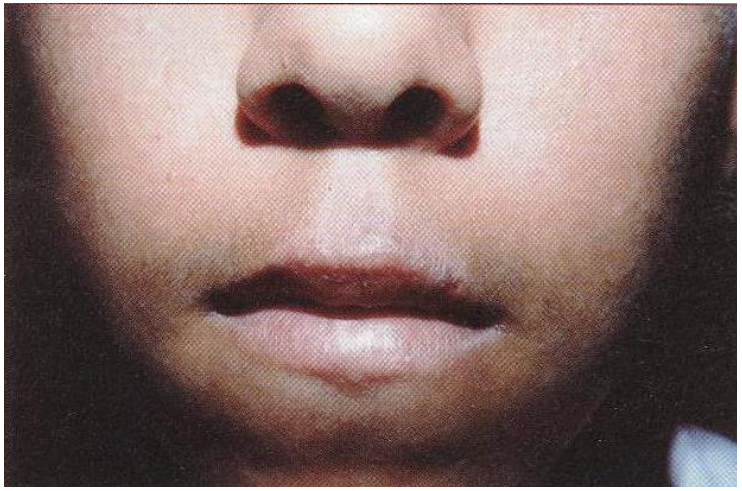
Substâncias alergenas

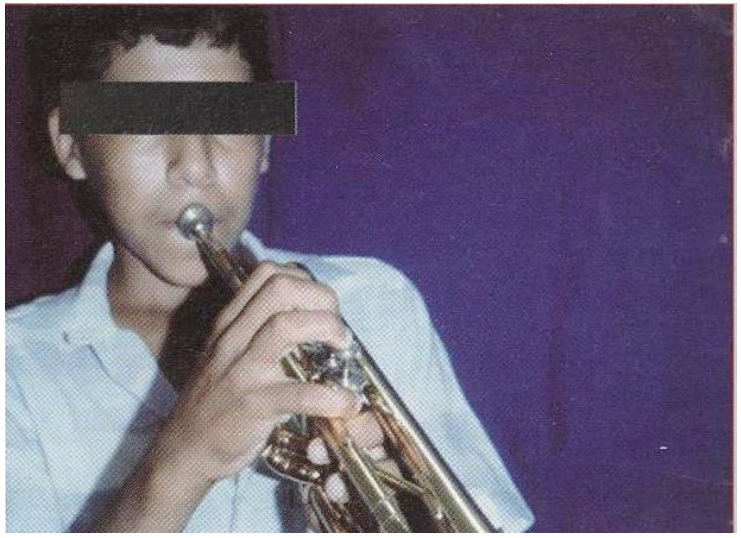
Tabela 47.1. Relação de Contactantes segundo a Região Acometida pela Dermatite

Localização	Contactantes (substância alergênica)
Pálpebras	Esmalte de unha, cosméticos [conservantes, fragrâncias], alérgenos aéreos [pó de madeira, pólen, sabões em pó], colírios
Orelhas ou região cervical	Bijuterias (níquel e cobalto), perfumes, *sprays* para cabelos, golas de roupas, óculos, aparelhos auditivos
Região frontal, couro cabeludo	Tintura para cabelo (parafenilenodiamina), xampus, *sprays* para cabelos, chapéus
Lábios, cavidade oral	Dentifrícios e soluções bucais, cosméticos, amálgama, próteses, instrumentos de sopro
Face	Cosméticos, loções para barba, alérgenos aéreos
Axila • Oco axilar • Região periaxilar	 Desodorantes e cremes depilatórios Tinturas de roupas
Antebraços	Bijuterias, alças de bolsas, sabões em pó, reveladores fotográficos (parafenilenodiamina), farinha de trigo (α-amilase)
Mãos	Luvas, utensílios domésticos [componentes de borracha e de plástico (mercaptobenzotiazol, thiurans)], metal, contato profissional [cimento (bicromato de potássio)], detergentes (níquel), aliáceas, plantas
Cintura	Elástico de roupas
Área de fraldas Genitais, região anal	Urina e fezes, cremes, componentes da fralda Tópicos, amaciantes de roupa, preservativos
Membros inferiores e pés	Cremes depilatórios, tópicos, calçados [componentes de borracha, plástico, couro, cola]

Dermatites de Contato

Metal





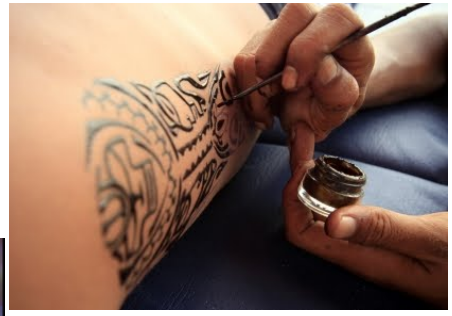
Couro

Dermatite de Contato ao Latex

Dermatite de Contato a Corantes

P-fenilenodiamina – PPD

- ✓ Corante de cabelo, “henna negra”



Dermatites de Contato

Perfume

- Cinamaldeído

Unhas postiças

- Cola

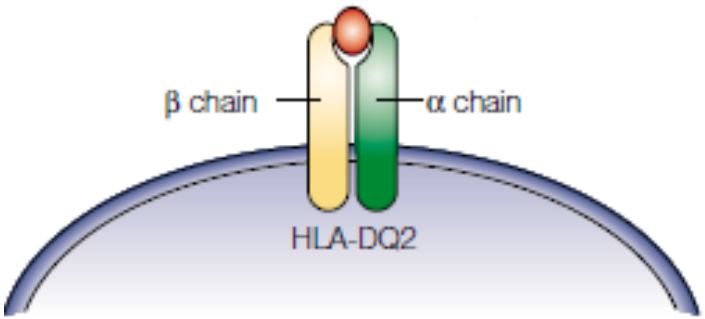
Tratamento para Hipersensibilidades de contato

- ✓ **Evitar o irritante ou alérgeno:** utilizar produtos hipoalergênicos (esmalte, tintura de cabelo), usar luvas de silicone, cremes de barreiras (silicone 5%)
- ✓.
- ✓ Compressas de permanganato de potássio e pasta d'água (fase aguda);
- ✓ Corticoides tópicos (pomada) e anti-histamínicos;
- ✓ Corticoides sistêmicos (ex: prednisona) dependendo da extensão do quadro.

Doença Celíaca

- Doença crônica da parte superior do intestino delgado
- Causada pela ingestão de glúten (complexo proteico presente no trigo, aveia e cevada)
- Fatores genéticos:

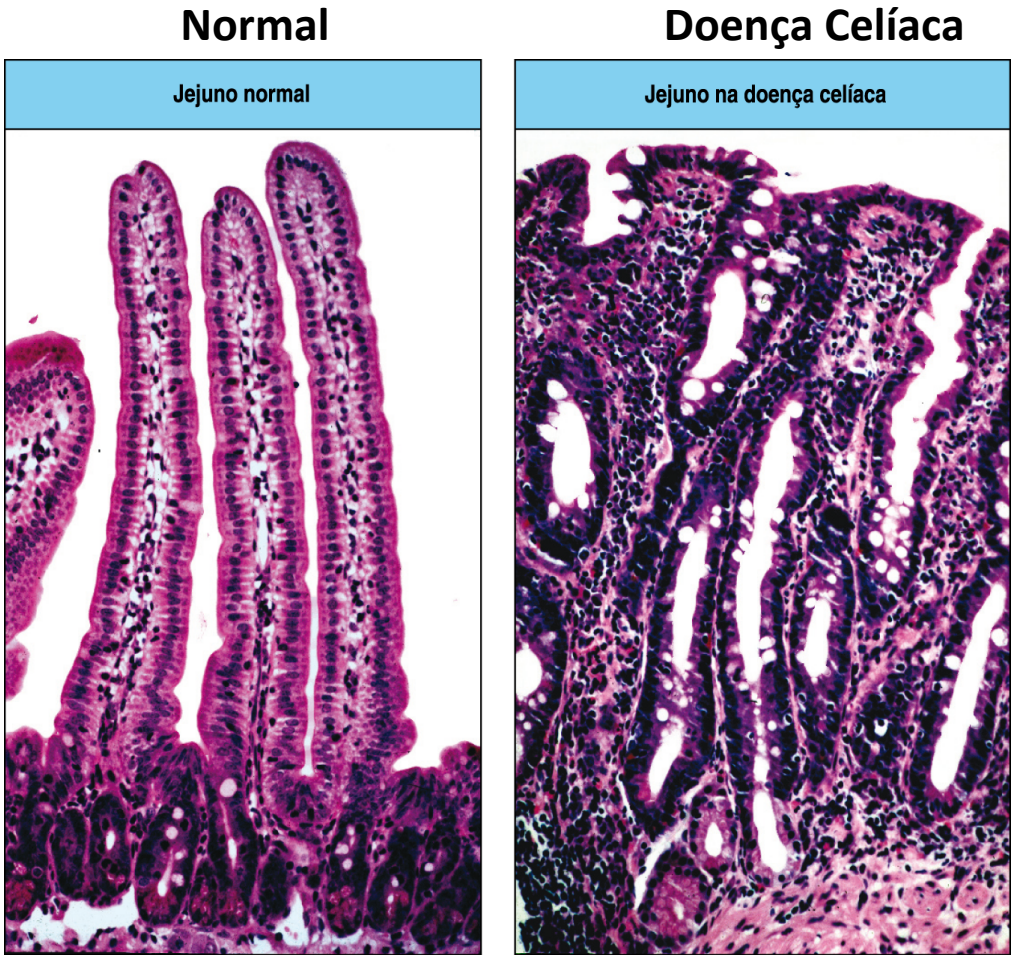
Alelo HLA-DQ2 do MHC de classe II → 95% do pacientes



Adaptado de Sollid, 2002

Caractaristicas Clínicas da DC

- Atrofia vilosa,
- Hiperplasia de cripta,
- Má absorção de alimentos,
- Diarreia crônica,
- Distensão abdominal,
- Perda de peso,
- Déficit de crescimento



Células TCD4 específicas para Glúten

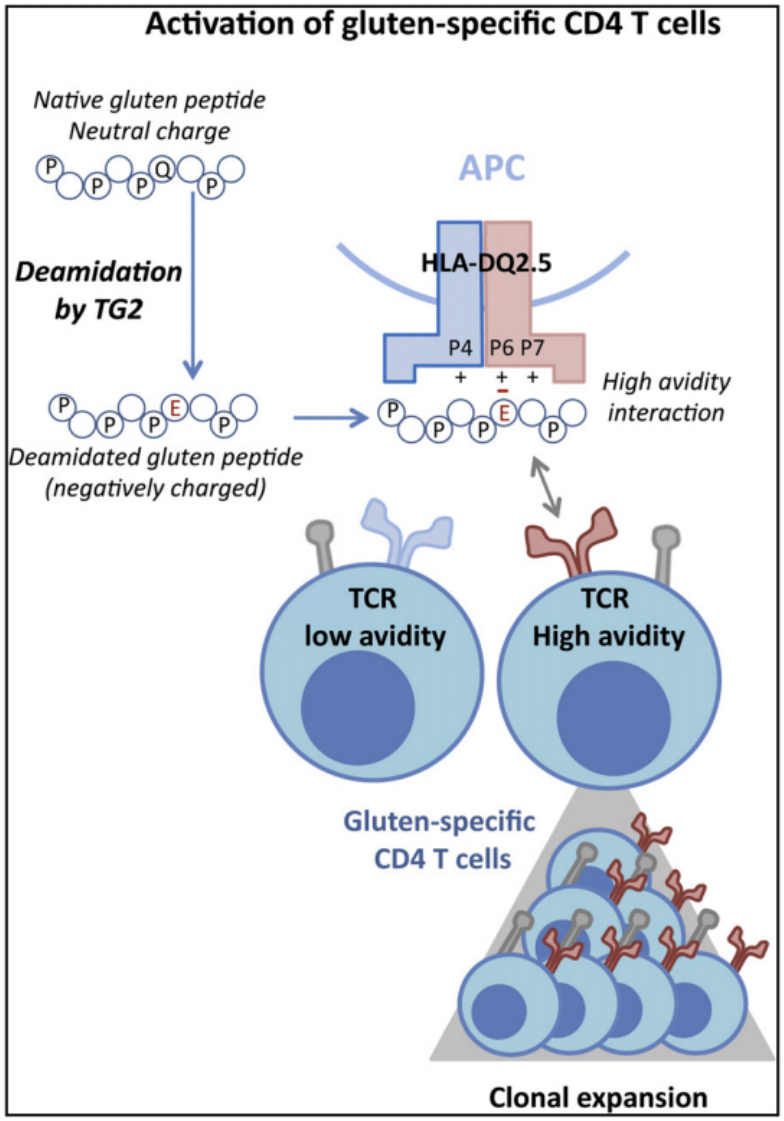


Figure 2. Activation of Gluten-Specific CD4⁺ T Cell Responses by HLA-DQ2.5 Molecule

Transglutaminase 2 (TG2) binds to and deamidates glutamine residues in Q-X-P sequences of gluten peptides into glutamic acid, introducing a negative charge that can interact with a positively charged lysine residue in position 6 of the peptide pocket of HLA-DQ2.5, resulting in enhanced peptide avidity for HLA-DQ2.5. HLA-DQ2.5-gluten peptide complexes expressed on antigen-presenting cells (APCs) can prime gluten-specific CD4 T cells. As for other dietary antigens, priming may occur in Peyer's patches or in mesenteric lymph nodes after migration of CD103⁺ dendritic cells loaded with gluten peptides in lamina propria (Worbs et al., 2006). Unusual priming outside the gut has however been reported in HLA-DQ2 mice (Du Pré et al., 2011). Priming is followed by selection and clonal expansion of T cells diplaying high-avidity TCR (Qiao et al., 2011).

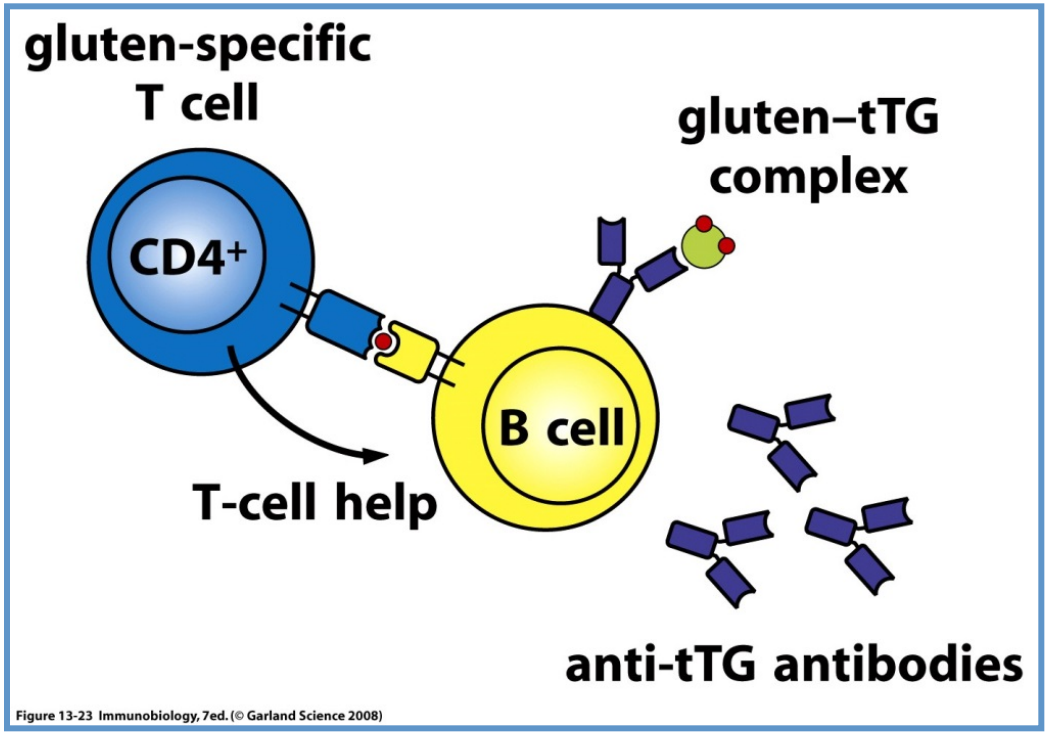
Meresse et al., *Immunity* 36, June 29, 2012

Doença celíaca

- Produção autoanticorpos

✓ **IgG e IgA**: contra transglutaminase tecidual

✓Não há células T específicas para a transglutaminase tecidual



*** tTG** = Enzima transglutaminase tecidual

Tratamento para DC

Evitar o alergeno

Estudar

- Janeway: Cap 13 pags 576-578; 583-590;
- Abbas: cap 18, pags 413 – 422.
- Imunologia Clínica na Prática Médica