Autoimmune Diseases

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Outline:
- intro
- classifications
- examples & treatments

Learning Objectives:
- autoimmune disease
- classifications
- mechanisms
- examples
- immunomodulatory drugs

*Ab-mediated autoimmunity can be transferred to baby
*T-mediated autoimmunity cannot be transferred to baby

*almost all rheumatic diseases are caused by autoimmunity

AUTOIMMUNE DISEASE - chronic, adaptive immune response against self; failure of self-tolerance; specific/non-specific
- *women > men*
- *5% in developed countries*
- *rarely resolved*

Self-Tolerance Mechanisms
- negative selection
- tissue-specific proteins in thymus
- no lymphocyte access to some tissues
- Treg
- anergy

CORTICOSTEROIDS - suppresses inflammation
CYCLOSPORINE - ↓T-cell activity
RITUXIMAB - α-CD20 mAb
CYCLOPHOSPHAMIDE - alkylating agent

PYRIDOSTIGMINE - prevents ACh degradation

Classification of Autoimmunity

Type 2

Disease	Ag	Result	Tx
Hemolytic Anemia	Rh	hemolysis by complement & phagocytosis	- transfusion - plasmapheresis - Immune Suppressors: - corticosteroids - cyclosporine - rituximab
Autoimmune Thrombocytopenia Pupura	GPIIb/IIIa	bleeding	
Goodpasture's	basement membrane collagen IV	glomerulonephritis, pulmonary hemorrhage	- plasmapheresis - Immune Suppressors: - cyclophosphamide - prednisone - rituximab
Pemphigus Vulgaris	epidermal cadherin	blisters	
Acute Rheumatoid Fever	steptococcal cell wall Ag causes Ab cross-rxn with cardiac muscle	arthritis, myocarditis, valve scarring	
Graves'	TSH-R (agonist)	hyperthyroidism	- propylthiouracil/methimazole - radioactive therapy (years): (can cause hypothyroidism) (on synthroid for life)
Hashimoto's	Thyroid	inflammation (goiter), hypothyroidism	- synthroid
Myastenia Gravis	ACh-R (antagonist)	weakness	- plasmapheresis - pyridostigmine - Immune Suppressors: - azathioprine - prednisone - thymectomy
DM2	Insulin receptor (antagonist)	hyperglycemia, ketoacidosis	
Hypoglycemia	Insulin receptor (agonist)	hypoglycemia	

Type 3 (Systemic)

Disease	Ag	Result	Tx
Subacute Bacterial Endocarditis	bacteria	glomerulonephritis	
Mixed Essential Cryoglobulinemia	rheumatoid Factor IgG complexes	systemic vasculitis	
Systemic Lupus Erythematosus	DNA, histones, ribosomes, snRNP/scRNP	glomerulonephritis, vasculitis, arthritis	- Immune Suppressors: - NSAIDs - corticosteroids - hydroxychloroquine - azathioprine - belimumab

Type 4

Disease	Ag	Result	Tx
DM1	β-cell	β-cell destruction	- insulin (inject, pump, inhale)
Rheumatoid Arthritis	unknown joint Ag	joint inflammation	- Immune Suppressors: - NAIDs - corticosteroids - hydroxychloroquine - methotrexate - abatacept (Orencia) - tocilizumab (Actemra) - infliximab (Remicade) - adalimumab (Humira) - etanercept (Enbrel) - certolizumab pegol (Cimzia)
MS	myelin protein, proteolipid protein	brain damage, paralysis	- plasmapheresis - Type 1 IFN - glatiramer acetate (Copaxone) - dimethyl fumarate (Tecfidera) - fingolimod (Gilenya) - natalizumab (Tysabri)

			- Immune Suppressors: - prednisone

Drugs that cause Autoimmunity (Lupus)
- hydralazine
- procainamide
- quinidine
- minocycline
- TNF-inhibitors** (drug that is used to treat autoimmunity & should work)