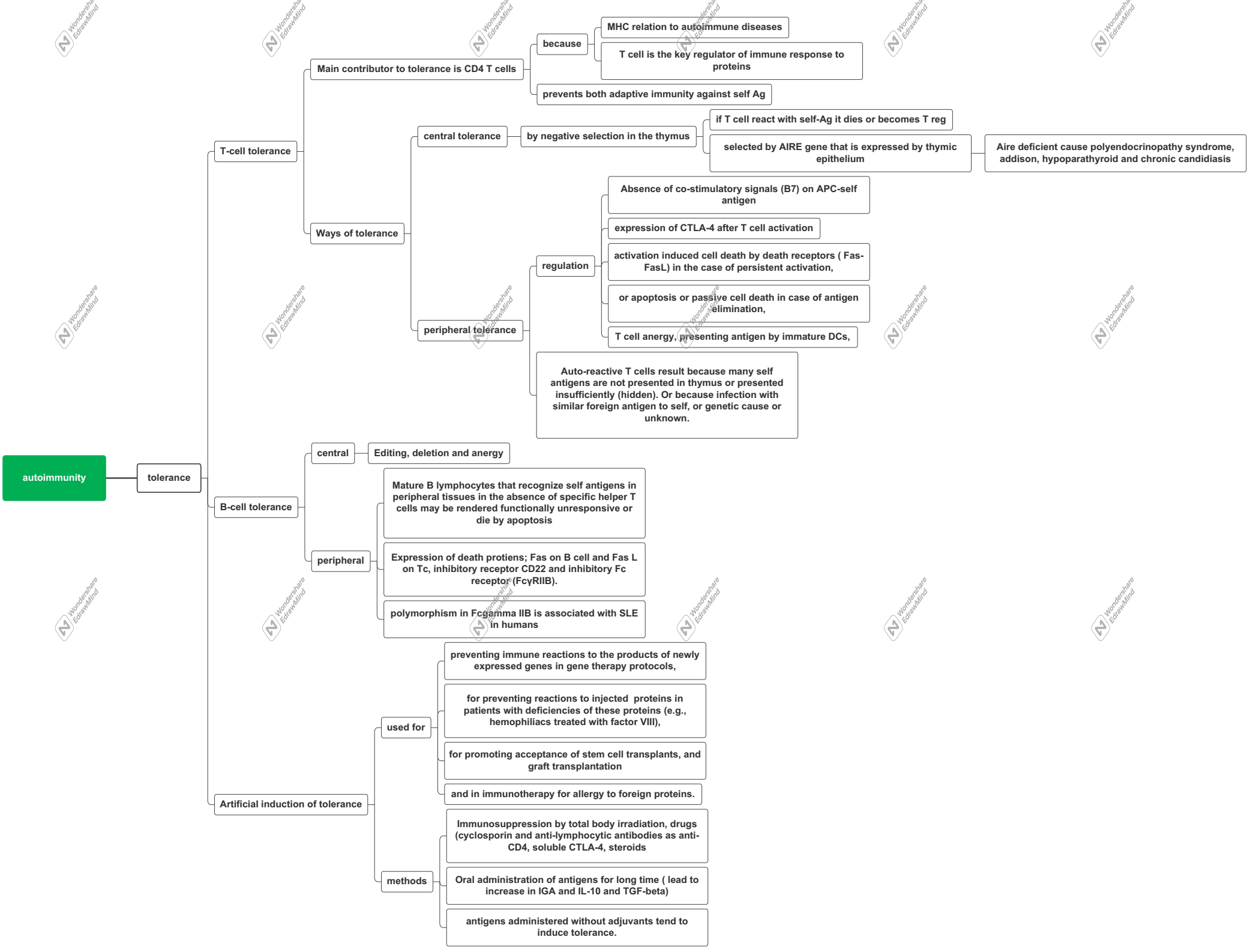
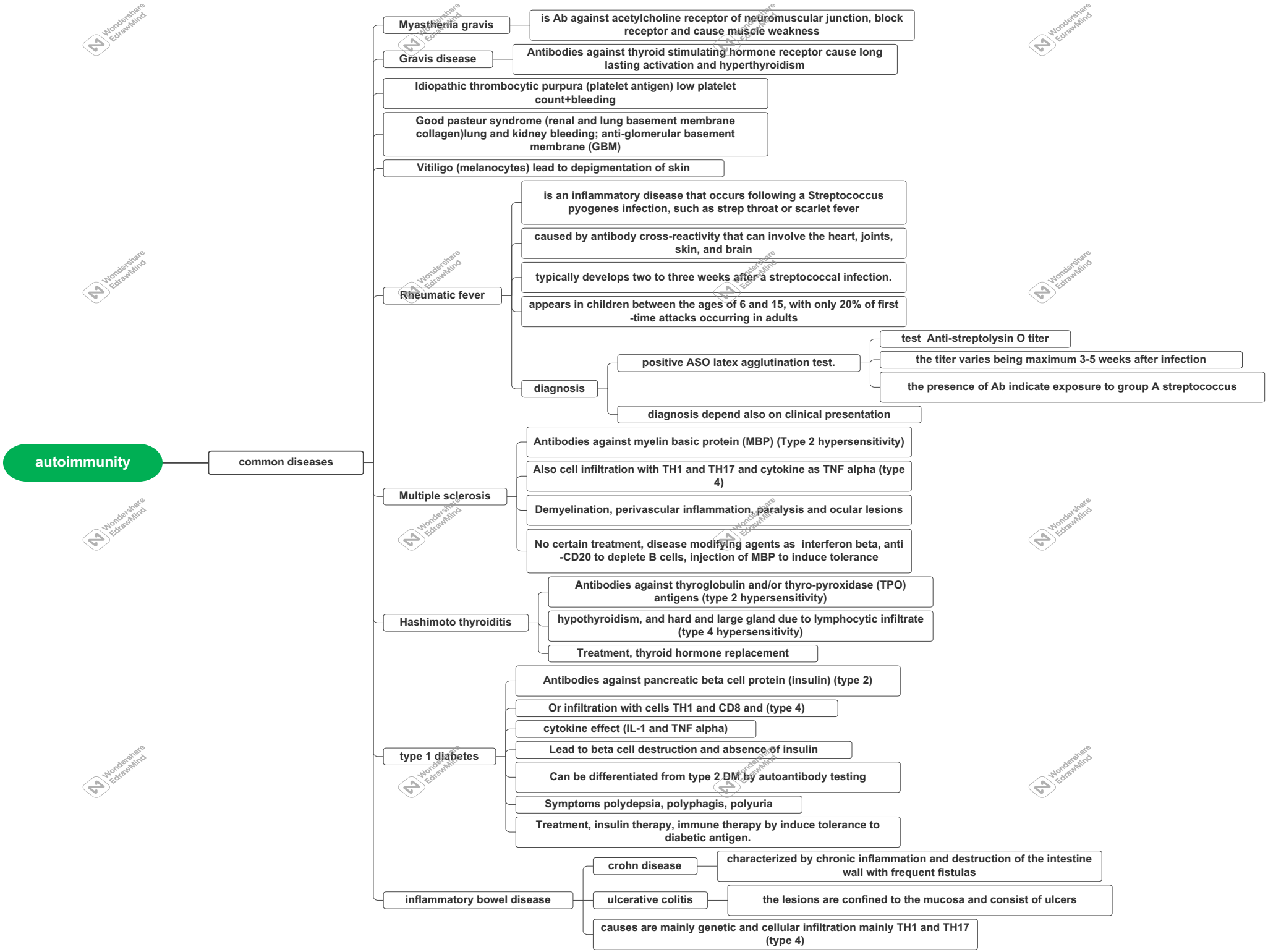

autoimmunity
tolerance
T-cell tolerance
Main contributor to tolerance is CD4 T cells
because
MHC relation to autoimmune diseases
T cell is the key regulator of immune response to proteins
prevents both adaptive immunity against self Ag
Ways of tolerance
central tolerance
by negative selection in the thymus
if T cell react with self-Ag it dies or becomes T reg
selected by AIRE gene that is expressed by thymic epithelium
Aire deficient cause polyendocrinopathy syndrome, addison, hypoparathyroid and chronic candidiasis
peripheral tolerance
regulation
Absence of co-stimulatory signals (B7) on APC-self antigen
expression of CTLA-4 after T cell activation
activation induced cell death by death receptors (Fas-FasL) in the case of persistent activation,
or apoptosis or passive cell death in case of antigen elimination,
T cell anergy, presenting antigen by immature DCs,
Auto-reactive T cells result because many self antigens are not presented in thymus or presented insufficiently (hidden). Or because infection with similar foreign antigen to self, or genetic cause or unknown.
B-cell tolerance
central
Editing, deletion and anergy
peripheral
Mature B lymphocytes that recognize self antigens in peripheral tissues in the absence of specific helper T cells may be rendered functionally unresponsive or die by apoptosis
Expression of death protiens; Fas on B cell and Fas L on Tc, inhibitory receptor CD22 and inhibitory Fc receptor (FcγRIIB).
polymorphism in Fcgamma IIB is associated with SLE in humans
Artificial induction of tolerance
used for
preventing immune reactions to the products of newly expressed genes in gene therapy protocols,
for preventing reactions to injected proteins in patients with deficiencies of these proteins (e.g., hemophiliacs treated with factor VIII),
for promoting acceptance of stem cell transplants, and graft transplantation
and in immunotherapy for allergy to foreign proteins.
methods
Immunosuppression by total body irradiation, drugs (cyclosporin and anti-lymphocytic antibodies as anti-CD4, soluble CTLA-4, steroids
Oral administration of antigens for long time (lead to increase in IGA and IL-10 and TGF-beta)
antigens administered without adjuvants tend to induce tolerance.


autoimmunity
common diseases
Myasthenia gravis
is Ab against acetylcholine receptor of neuromuscular junction, block receptor and cause muscle weakness
Gravis disease
Antibodies against thyroid stimulating hormone receptor cause long lasting activation and hyperthyroidism
Idiopathic thrombocytic purpura (platelet antigen) low platelet count+bleeding
Good pasteur syndrome (renal and lung basement membrane collagen)lung and kidney bleeding; anti-glomerular basement membrane (GBM)
Vitiligo (melanocytes) lead to depigmentation of skin
Rheumatic fever
is an inflammatory disease that occurs following a Streptococcus pyogenes infection, such as strep throat or scarlet fever
caused by antibody cross-reactivity that can involve the heart, joints, skin, and brain
typically develops two to three weeks after a streptococcal infection.
appears in children between the ages of 6 and 15, with only 20% of first -time attacks occurring in adults
diagnosis
positive ASO latex agglutination test.
test Anti-streptolysin O titer
the titer varies being maximum 3-5 weeks after infection
the presence of Ab indicate exposure to group A streptococcus
diagnosis depend also on clinical presentation
Multiple sclerosis
Antibodies against myelin basic protein (MBP) (Type 2 hypersensitivity)
Also cell infiltration with TH1 and TH17 and cytokine as TNF alpha (type 4)
Demyelination, perivascular inflammation, paralysis and ocular lesions
No certain treatment, disease modifying agents as interferon beta, anti -CD20 to deplete B cells, injection of MBP to induce tolerance
Hashimoto thyroiditis
Antibodies against thyroglobulin and/or thyro-pyroxidase (TPO) antigens (type 2 hypersensitivity)
hypothyroidism, and hard and large gland due to lymphocytic infiltrate (type 4 hypersensitivity)
Treatment, thyroid hormone replacement
type 1 diabetes
Antibodies against pancreatic beta cell protein (insulin) (type 2)
Or infiltration with cells TH1 and CD8 and (type 4)
cytokine effect (IL-1 and TNF alpha)
Lead to beta cell destruction and absence of insulin
Can be differentiated from type 2 DM by autoantibody testing
Symptoms polydepsia, polyphagis, polyuria
Treatment, insulin therapy, immune therapy by induce tolerance to diabetic antigen.
inflammatory bowel disease
crohn disease
characterized by chronic inflammation and destruction of the intestine wall with frequent fistulas
ulcerative colitis
the lesions are confined to the mucosa and consist of ulcers
causes are mainly genetic and cellular infiltration mainly TH1 and TH17 (type 4)