

Myasthenia gravis

Case Study

Myasthenia gravis

My= muscle, asthenia= weakness, gravis= severe

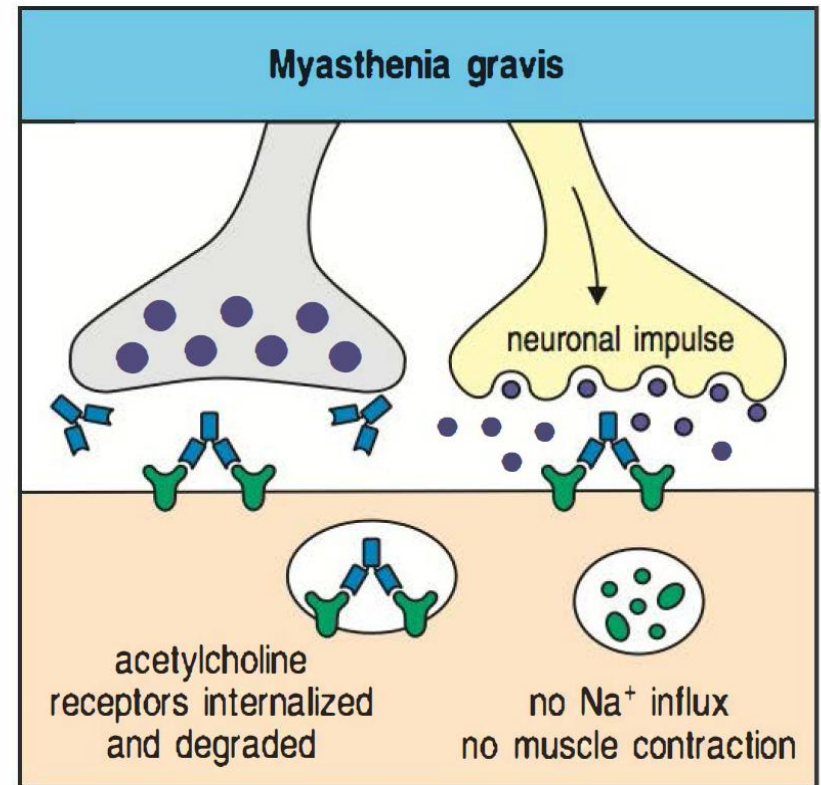
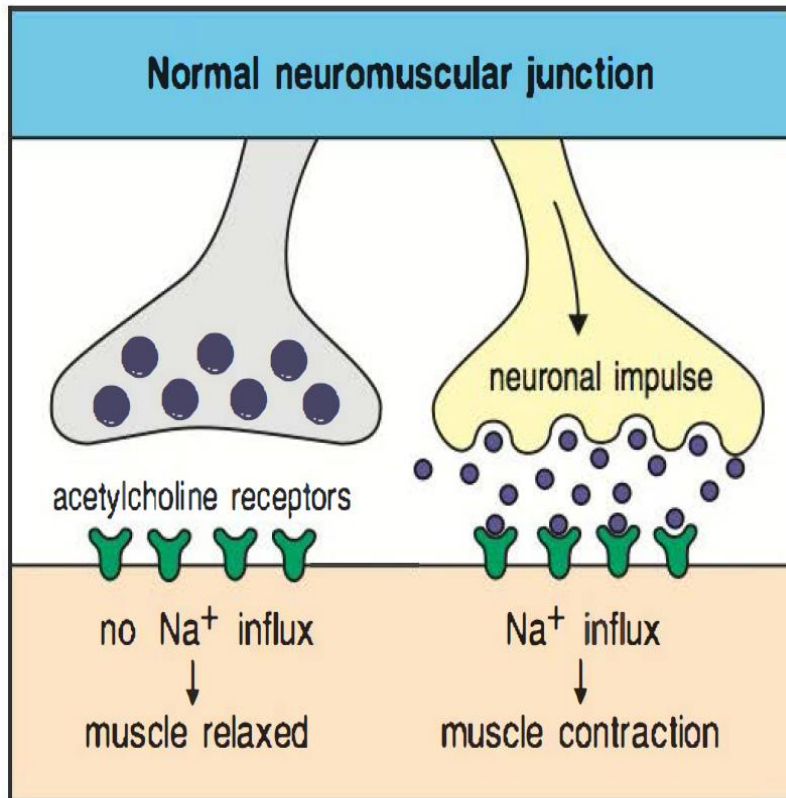
Type II IgG-mediated autoimmune disease.

Mediated by autoantibodies against Acetylcholine receptors.

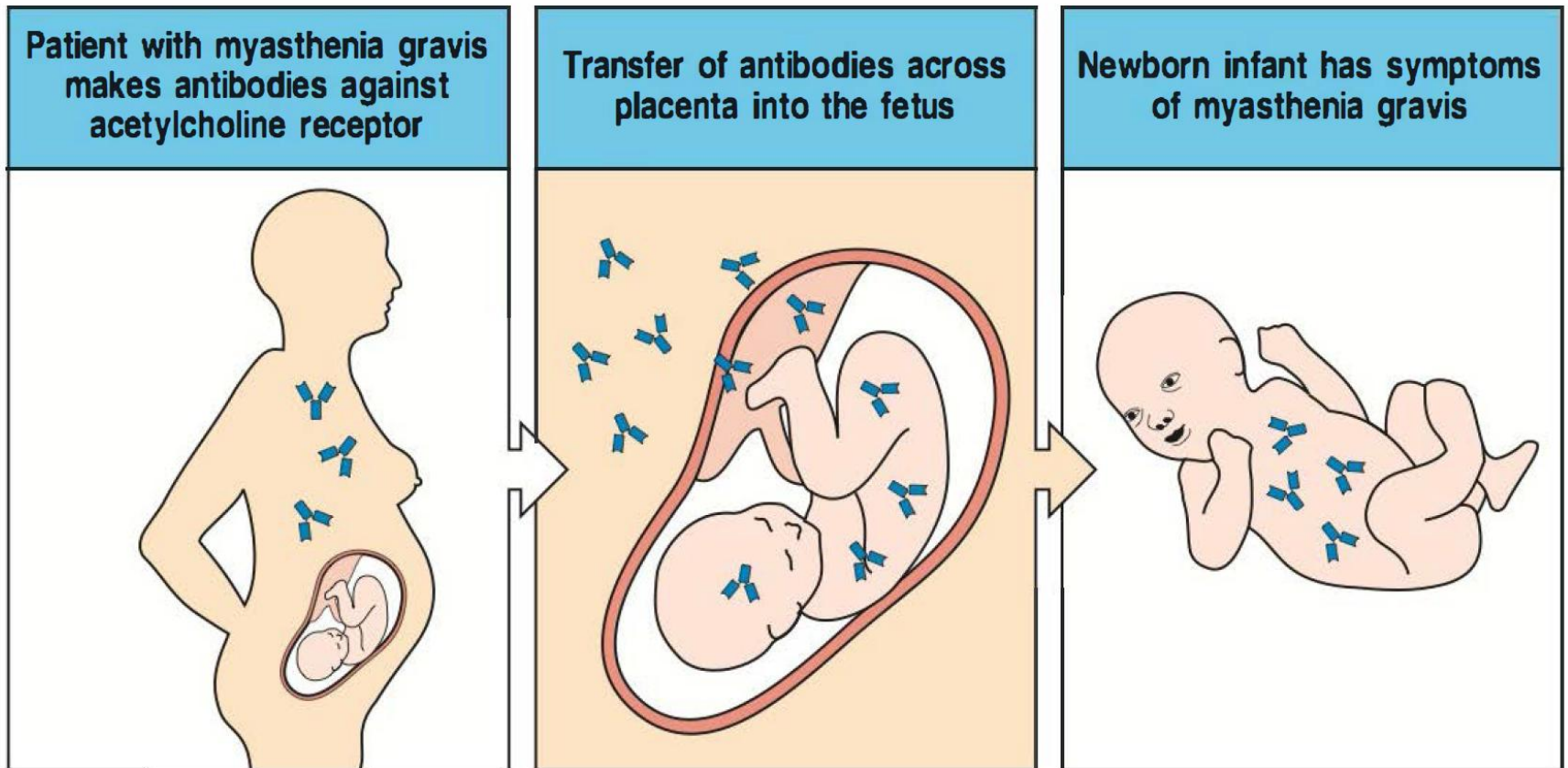
Examples of type II autoimmune diseases

Some common type II autoimmune diseases caused by antibody against surface or matrix antigens		
Syndrome	Autoantigen	Consequence
Autoimmune hemolytic anemia (see Case 41)	Rh blood group antigens, I antigen	Destruction of red blood cells by complement and phagocytes, anemia
Autoimmune thrombocytopenic purpura	Platelet integrin GpIIb/IIIa	Abnormal bleeding
Goodpasture's syndrome	Noncollagenous domain of basement membrane collagen type IV	Glomerulonephritis Pulmonary hemorrhage
Pemphigus vulgaris (see Case 43)	Epidermal cadherin	Blistering of skin
Graves' disease	Thyroid-stimulating hormone receptor	Hyperthyroidism
Myasthenia gravis	Acetylcholine receptor	Progressive weakness
Insulin-resistant diabetes	Insulin receptor (antagonist)	Hyperglycemia, ketoacidosis
Hypoglycemia	Insulin receptor (agonist)	Hypoglycemia

Myasthenia gravis mode of action



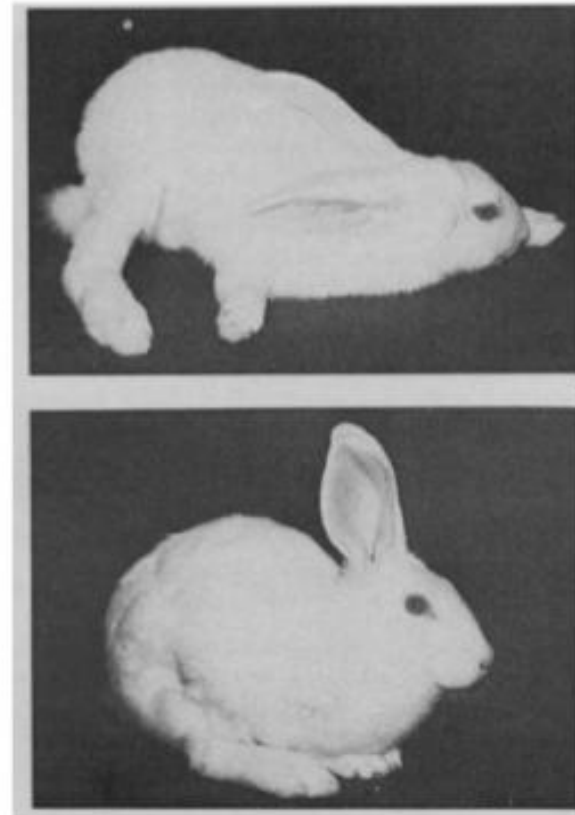
Myasthenia Gravis can be transferred to newborns



Antibodies against AChR effect on rabbits

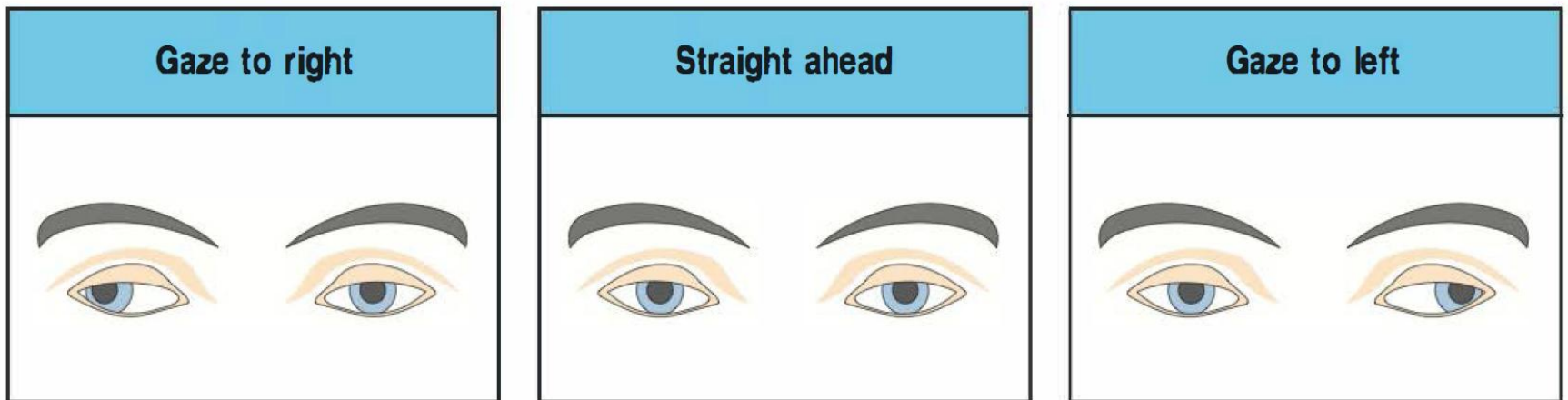
- Rabbits (N=7) received injections of acetylcholine receptor from electric eel
- Paralysis (top) is reversed by increasing ACh (bottom)

Electrophorus electricus



Patrick & Lindstrom (1973). Science, 180(4088), 871-872.

Drooping eyelid and ocular movement limitations



Case of Mr. Weld

71 year-old, diplopia and ptosis

Limitations in ocular movement

No Thymus enlargement

Positive for Acetylcholine receptor antibodies

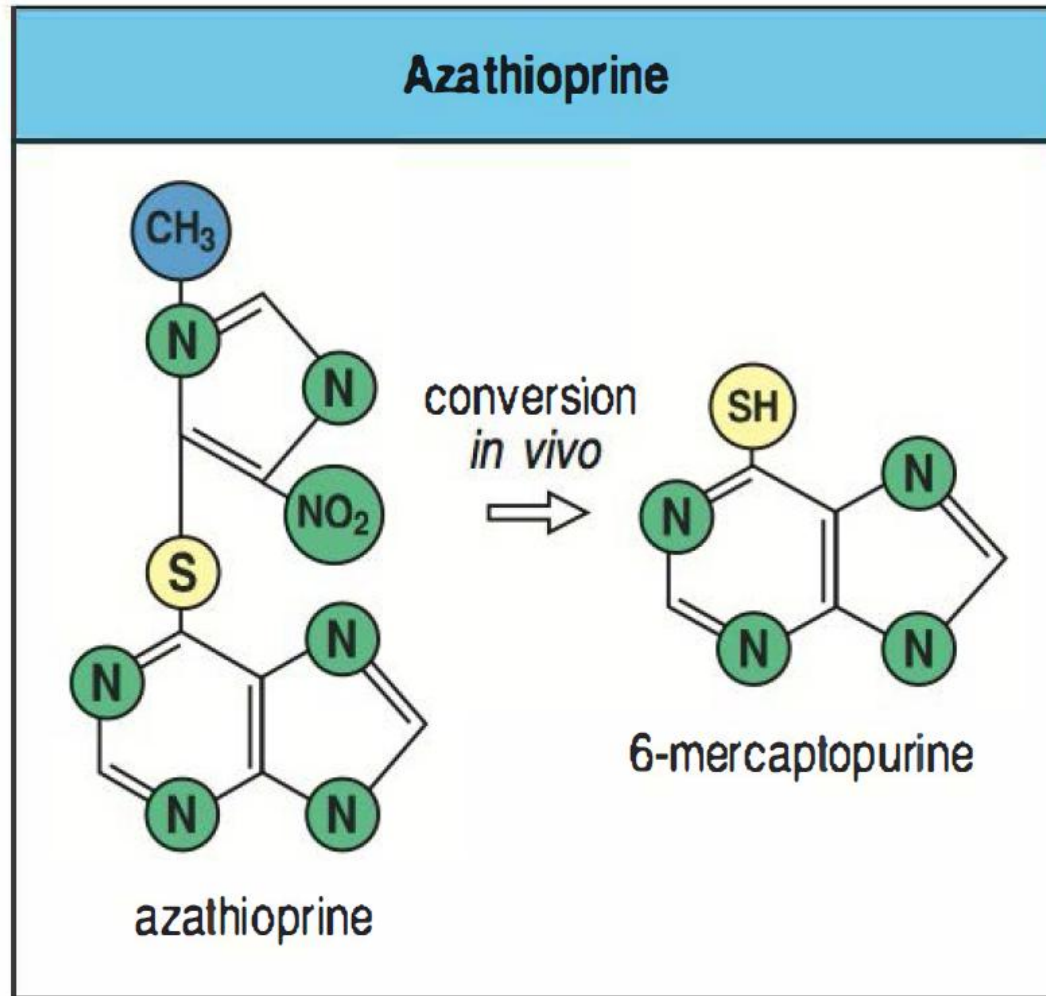
Pyridostigmine (Acetylcholinesterase inhibitor), caused him diarrhea, dose limited

3 years later, following a severe respiratory infection, symptoms returned and more strongly

Speech affected, chewing and swallowing became difficult, also breathing difficulties

Treated with Azathioprine in hospital, steady improvement

Azathioprine



An immunosuppressive agent that block DNA synthesis

How long do Myasthenia Gravis symptoms last in infants?

1-2 weeks

How does pyridostigmine work?

Inhibits acetylcholinesterase

Why is diarrhea a common side effect of pyridostigmine?

Increased amounts of acetylcholine in intestines causes increased binding to muscarinic receptors in intestines, increasing intestinal motility.

How does Azathioprine work, any side effects?

It inhibits proliferation of B and T cells. Non-specific, makes patient more susceptible to infections. Long-term use is associated with lymphomas.

Severe relapse after infection, why?

Mechanism	Disruption of cell or tissue barrier	Infection of antigen-presenting cell	Binding of pathogen to self protein	Molecular mimicry	Superantigen
Effect	Release of sequestered self antigen; activation of nontolerized cells	Induction of co-stimulatory activity on antigen-presenting cells	Pathogen acts as carrier to allow anti-self response	Production of cross-reactive antibodies or T cells	Polyclonal activation of autoreactive T cells
Example	Sympathetic ophthalmia	Effect of adjuvants in induction of EAE	? Interstitial nephritis	Rheumatic fever ? Diabetes ? Multiple sclerosis	? Rheumatoid arthritis