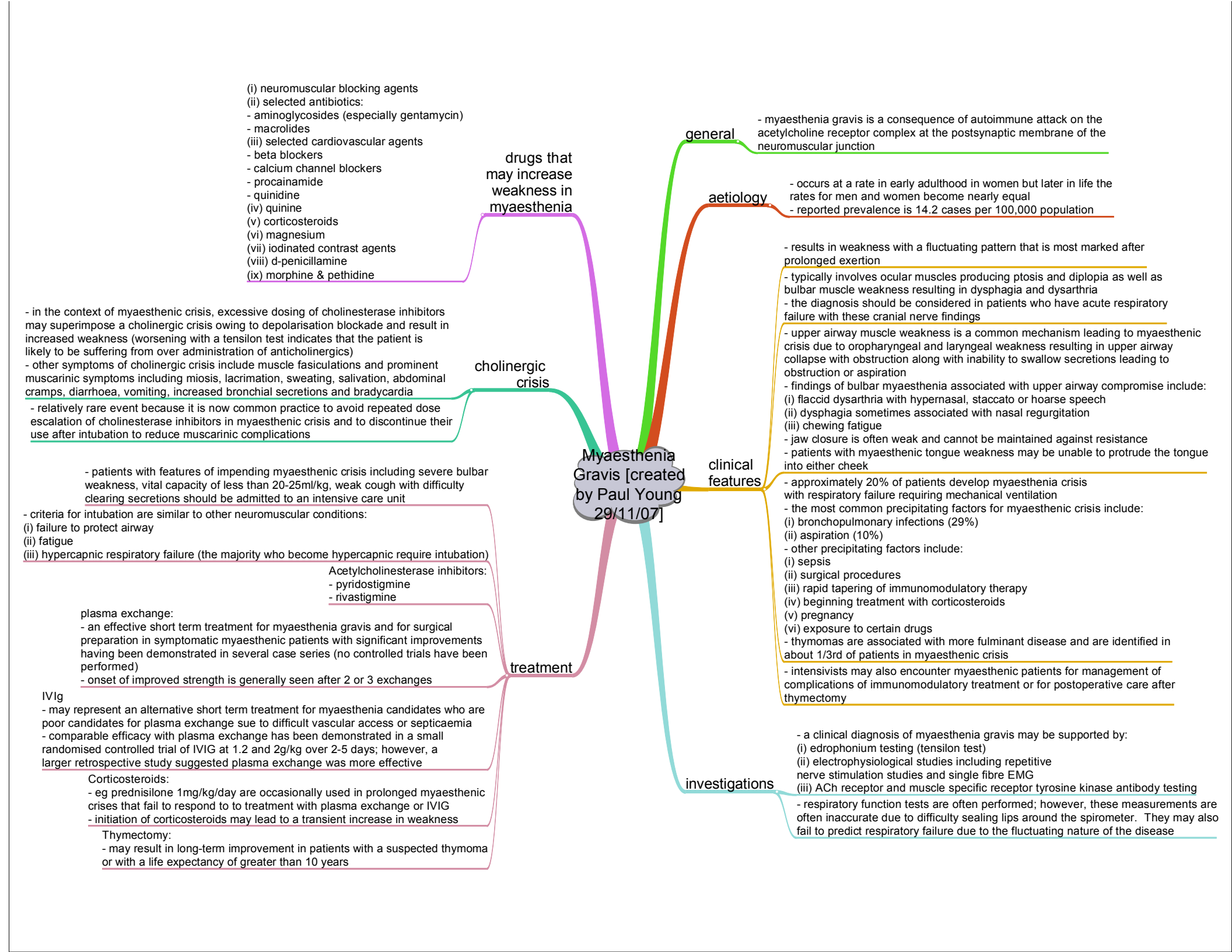
Myaesthenia Gravis [created by Paul Young 29/11/07]
general
- myaesthenia gravis is a consequence of autoimmune attack on the acetylcholine receptor complex at the postsynaptic membrane of the neuromuscular junction
aetiology
- occurs at a rate in early adulthood in women but later in life the rates for men and women become nearly equal
- reported prevalence is 14.2 cases per 100,000 population
clinical features
- results in weakness with a fluctuating pattern that is most marked after prolonged exertion
- typically involves ocular muscles producing ptosis and diplopia as well as bulbar muscle weakness resulting in dysphagia and dysarthria
- the diagnosis should be considered in patients who have acute respiratory failure with these cranial nerve findings
- upper airway muscle weakness is a common mechanism leading to myaesthenic crisis due to oropharyngeal and laryngeal weakness resulting in upper airway collapse with obstruction along with inability to swallow secretions leading to obstruction or aspiration
- findings of bulbar myaesthenia associated with upper airway compromise include:
(i) flaccid dysarthria with hypernasal, staccato or hoarse speech
(ii) dysphagia sometimes associated with nasal regurgitation
(iii) chewing fatigue
- jaw closure is often weak and cannot be maintained against resistance
- patients with myaesthenic tongue weakness may be unable to protrude the tongue into either cheek
- approximately 20% of patients develop myaesthenia crisis with respiratory failure requiring mechanical ventilation
- the most common precipitating factors for myaesthenic crisis include:
(i) bronchopulmonary infections (29%)
(ii) aspiration (10%)
- other precipitating factors include:
(i) sepsis
(ii) surgical procedures
(iii) rapid tapering of immunomodulatory therapy
(iv) beginning treatment with corticosteroids
(v) pregnancy
(vi) exposure to certain drugs
- thymomas are associated with more fulminant disease and are identified in about 1/3rd of patients in myaesthenic crisis
- intensivists may also encounter myaesthenic patients for management of complications of immunomodulatory treatment or for postoperative care after thymectomy
investigations
- a clinical diagnosis of myaesthenia gravis may be supported by:
(i) edrophonium testing (tensilon test)
(ii) electrophysiological studies including repetitive nerve stimulation studies and single fibre EMG
(iii) ACh receptor and muscle specific receptor tyrosine kinase antibody testing
- respiratory function tests are often performed; however, these measurements are often inaccurate due to difficulty sealing lips around the spirometer. They may also fail to predict respiratory failure due to the fluctuating nature of the disease
treatment
- patients with features of impending myaesthenic crisis including severe bulbar weakness, vital capacity of less than 20-25ml/kg, weak cough with difficulty clearing secretions should be admitted to an intensive care unit
- criteria for intubation are similar to other neuromuscular conditions:
(i) failure to protect airway
(ii) fatigue
(iii) hypercapnic respiratory failure (the majority who become hypercapnic require intubation)
Acetylcholinesterase inhibitors:
- pyridostigmine
- rivastigmine
plasma exchange:
- an effective short term treatment for myaesthenia gravis and for surgical preparation in symptomatic myaesthenic patients with significant improvements having been demonstrated in several case series (no controlled trials have been performed)
- onset of improved strength is generally seen after 2 or 3 exchanges
IVIg
- may represent an alternative short term treatment for myaesthenia candidates who are poor candidates for plasma exchange sue to difficult vascular access or septicaemia
- comparable efficacy with plasma exchange has been demonstrated in a small randomised controlled trial of IVIG at 1.2 and 2g/kg over 2-5 days; however, a larger retrospective study suggested plasma exchange was more effective
Corticosteroids:
- eg prednisilone 1mg/kg/day are occasionally used in prolonged myaesthenic crises that fail to respond to to treatment with plasma exchange or IVIG
- initiation of corticosteroids may lead to a transient increase in weakness
Thymectomy:
- may result in long-term improvement in patients with a suspected thymoma or with a life expectancy of greater than 10 years
cholinergic crisis
- in the context of myaesthenic crisis, excessive dosing of cholinesterase inhibitors may superimpose a cholinergic crisis owing to depolarisation blockade and result in increased weakness (worsening with a tensilon test indicates that the patient is likely to be suffering from over administration of anticholinergics)
- other symptoms of cholinergic crisis include muscle fasiculations and prominent muscarinic symptoms including miosis, lacrimation, sweating, salivation, abdominal cramps, diarrhoea, vomiting, increased bronchial secretions and bradycardia
- relatively rare event because it is now common practice to avoid repeated dose escalation of cholinesterase inhibitors in myaesthenic crisis and to discontinue their use after intubation to reduce muscarinic complications
drugs that may increase weakness in myaesthenia
(i) neuromuscular blocking agents
(ii) selected antibiotics:
- aminoglycosides (especially gentamycin)
- macrolides
(iii) selected cardiovascular agents
- beta blockers
- calcium channel blockers
- procainamide
- quinidine
(iv) quinine
(v) corticosteroids
(vi) magnesium
(vii) iodinated contrast agents
(viii) d-penicillamine
(ix) morphine & pethidine