Anaesthetising the thyrotoxic patient – for emergency surgery

Emma Lei Lei
Westmead Anaesthetic Departmental Talk
June 19th 2012
Focus of this talk

- Emergency non thyroid surgery
- Effect on CVS system
- Rapid preoperative optimisation
- Conduct of anaesthesia
- Management of thyroid storm
Case report

- 25yo male, MBA at 60kph, sustained left distal radial ulnar fracture and multiple open compound fractures of right hand with neurological compromise

- 1 year history of hyperthyroidism, known toxic nodule (5x5x5cm), untreated
  - Clinically thyrotoxic: HR 100-120, BP 150/50, 38°C, anxious, tremors
  - Biochemically thyrotoxic: TSH <0.04, T4 51, T3 9.4
  - Commenced on propanolol 20mg BD, neomercazole 20mg TDS, prednisolone 20mg daily on admission

- Require urgent surgery for fractures but endocrine advised unsafe for anaesthesia for 5 days until euthryoid, due to high risk of thyroid storm
  - Also advised fentanyl, tramadol and all NSAIDS are unsafe

- Had surgery for both upper limbs the next day under GA, against endocrine team's advice; uneventful GA

- Thyrotoxicosis improved over the next week, no thyroid storm
Introduction

- Thyrotoxicosis
  - State of thyroid hormone excess from any cause

- Hyperthyroidism
  - Increased thyroid hormone synthesis and secretion

- Epidemiology
  - Prevalence: US 1.3%; UK 2% in women, 0.2% in men
  - Incidence increase with age, white population, and in iodine deficient areas
  - Clinical thyrotoxicosis usually seen in young people
  - Elderly people tend to be subclinical
Thyroid physiology

- Thyroxine
  - 2 types T4, T3,
  - 2-3 months supply of stored preformed hormones in thyroid gland
  - Majority are protein bound but it is the free hormones that are physiologically active (large reservoir of hormones in circulation)

<table>
<thead>
<tr>
<th></th>
<th>T4</th>
<th>T3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Daily release</td>
<td>80ug (100nmol)</td>
<td>4ug (10nmol)</td>
</tr>
<tr>
<td>Total plasma level</td>
<td>5-20ug/dL (103nmol/L)</td>
<td>0.1-0.3ug/dL (2-5nmol/L)</td>
</tr>
<tr>
<td>Free hormone</td>
<td>10-30 pM/L</td>
<td>3-12 pM/L</td>
</tr>
<tr>
<td>Protein binding</td>
<td>99.9%; TBG, TBPA, albumin</td>
<td>99.7%; TBG, albumin</td>
</tr>
<tr>
<td>T1/2</td>
<td>7 days</td>
<td>1 day</td>
</tr>
</tbody>
</table>
Control of thyroid hormone release
Causes of thyrotoxicosis

- **Common causes**
  - Thyrotoxicosis associated with hyperthyroidism
    - Graves disease
    - Solitary toxic nodule
    - Toxic multi-nodular goiter
  - Thyrotoxicosis not associated with hyperthyroidism
    - Thyroiditis 10% e.g. silent thyroiditis
    - Postpartum thyroiditis
    - Sub-acute thyroiditis

- **Less common causes**
  - Thyrotoxicosis associated with hyperthyroidism
    - TSH secreting pituitary adenomas, pituitary resistance to thyroid hormone, thyroid cancer, drug induced
  - Thyrotoxicosis not associated with hyperthyroidism
    - Drug induced (e.g. amiodarone, IFa, lithium), radiation thyroiditis
Clinical manifestations of thyrotoxicosis

- Free T3 and T4 act predominantly on cell nucleus
  - Slow onset (hours); long duration (days)

- Thyrotoxicosis causes a bi-hormonal state involving increased thyroid hormones and catecholamines

- Metabolic
  - $\uparrow$ cell metabolism $\rightarrow$ $\uparrow$ BMR by $\uparrow$ cellular and Na-K ATPase activity
  - $\uparrow$ heat production
  - Hyperglycaemia from $\uparrow$ glucose absorption, GNG and glycolysis
  - $\uparrow$ lipolysis and free FA, $\downarrow$ cholesterol and TG
  - Anabolic at physiological levels but catabolic at high levels
  - Can lead to ketoacidosis, lactic acidosis
Cardiovascular

- Thyroid hormone and catecholamines are synergistic
- Acts on the heart, vasculature and adrenergic system
- Affect cardiac myocyte gene expression
- ↑ beta adrenergic activity by ↑ number of and affinity of beta-adrenergic receptors to catecholamines

<table>
<thead>
<tr>
<th>Cardiac parameter</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive inotropy and lusitropy</td>
<td>↑ a-MHC (myosin heavy chain) expression, which has greater ATPase activity → faster contraction</td>
</tr>
<tr>
<td>↑ CO</td>
<td>Up to 2-3x</td>
</tr>
<tr>
<td>↑ Cardiac work at rest</td>
<td></td>
</tr>
<tr>
<td>↑ HR</td>
<td>Usually sinus tachycardia</td>
</tr>
<tr>
<td></td>
<td>Atrial arrhythmia in up to 15%</td>
</tr>
<tr>
<td>↑ PVR</td>
<td>PAP increase up to 35-40mmHg</td>
</tr>
<tr>
<td>↓ SVR</td>
<td>Up to 50%; directly vasodilate vascular smooth muscle and release vasodilators e.g. NO</td>
</tr>
<tr>
<td></td>
<td>↑ blood flow to skin, muscles, liver, heart</td>
</tr>
<tr>
<td>↑ Blood volume</td>
<td>↓SVR → ↓renal perfusion pressure → ↑epo and activate RAAS (renal Na and water reabsorption)</td>
</tr>
</tbody>
</table>
Clinical manifestations of cardiovascular effects

- Resting sinus tachycardia
- Atrial arrhythmia in up to 15%, especially older patients
- Exercise intolerance
  - High CO at rest and blunted ↑ CO with exercise; myopathy of respiratory and skeletal muscles
- Angina
  - Ischemia from O2 supply demand imbalance and coronary artery spasm; may unmask CAD in older patients
- Cardiac failure
  - Rare, usually in older patients, prolonged and severe disease, or have underlying heart disease; worse in the presence of AF
  - High output heart failure can occur in young people; controversial
  - Rate related heart failure as sustained tachycardia impairs ventricular myocyte’s ability to regulate cytosolic calcium
<table>
<thead>
<tr>
<th>System</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>• Hyperactivity, irritability</td>
</tr>
<tr>
<td></td>
<td>• Insomnia and impaired concentration</td>
</tr>
<tr>
<td></td>
<td>• Hyperreflexic</td>
</tr>
<tr>
<td></td>
<td>• Hypokalaemic periodic paralysis</td>
</tr>
<tr>
<td>Eyes</td>
<td>• Graves eye signs</td>
</tr>
<tr>
<td>Thyroid and airway</td>
<td>• Upper airway compression</td>
</tr>
<tr>
<td></td>
<td>• Retrosternal extension and SVC obstruction</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>• Weight loss</td>
</tr>
<tr>
<td></td>
<td>• Increased appetite</td>
</tr>
<tr>
<td></td>
<td>• Diarrhea and ↑gastric motility</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>• Proximal myopathy due to protein catabolism</td>
</tr>
<tr>
<td></td>
<td>• Osteoporosis and ↑bone turnover</td>
</tr>
<tr>
<td>Dermatological</td>
<td>• Warm, sweating, heat intolerance</td>
</tr>
<tr>
<td></td>
<td>• Fine hair, diffuse alopecia</td>
</tr>
<tr>
<td></td>
<td>• Thyroid dermopathy</td>
</tr>
<tr>
<td></td>
<td>• Thyroid acropachy</td>
</tr>
<tr>
<td></td>
<td>• Pretibial myxoedema</td>
</tr>
<tr>
<td>Reproductive</td>
<td>• Male: impotence</td>
</tr>
<tr>
<td></td>
<td>• Female: oligomenorrhea</td>
</tr>
</tbody>
</table>
Diagnosis of thyrotoxicosis

- **Laboratory**
  - TSH: single best test of thyroid hormone action at cellular level, small change in thyroid function leads to significant change in TSH
  - Total T4, T3, rT3u, free T4, T3
  - TPO antibodies, TBII, TSI, serum antrimicrosomal antibodies, antithyroglobulin antibodies, thyroglobulin
  - TRH stimulation test

- **Imaging**
  - US, CT, MRI
  - Radioactive iodine uptake with $^{123}$I, $^{131}$I, Tc$^{99}$m

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>TSH</th>
<th>Total T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euthyroid</td>
<td>0.4 – 5mU/L</td>
<td>5-12ug/dL</td>
</tr>
<tr>
<td>Subclinical hyperthyroid</td>
<td>0.1-0.4mU/L</td>
<td>5-12ug/dL</td>
</tr>
<tr>
<td>Overt hyperthyroid</td>
<td>&lt;0.03mU/L</td>
<td>&gt;12ug/dL</td>
</tr>
<tr>
<td>Thyroid storm</td>
<td>&lt;0.01mU/L</td>
<td>&gt;12ug/dL</td>
</tr>
</tbody>
</table>
Anaesthetising the thyrotoxic patient

- American thyroid association and American Association of Clinical Endocrinologists recommend rendering euthyroid prior to surgery

- Sometimes this is not possible
  - Thyroidectomy for failed medical therapy
    - 3 in 1000 cannot take antithyroid drugs due to serious adverse effects
    - Refractory to maximal antithyroid drugs and radioablation
  - Emergency non-thyroid surgery
  - Newly diagnosed
Preoperative optimisation

- Goals

- 1. Render euthyroid
  - This takes time (6-8 weeks): $t_{1/2}$ of T4 is 7 days and a large store of preformed hormones in circulation and in thyroid gland
  - Prevent thyroid hormone synthesis, secretion, and peripheral conversion of T4 to T3

- 2. Block effects of thyroid hormone

- 3. Support and prevent systemic decompensation

- 4. Prevent thyroid storm
<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibition of hormone synthesis</td>
<td>Thionamide drugs e.g. PTU, MMI</td>
</tr>
<tr>
<td>Inhibition of hormone release</td>
<td>IV iodine</td>
</tr>
<tr>
<td></td>
<td>Oral: potassium iodide, Lugol’s solution, iopanoic acid</td>
</tr>
<tr>
<td></td>
<td>Lithium</td>
</tr>
<tr>
<td>Inhibition of conversion T4 to T3</td>
<td>PTU</td>
</tr>
<tr>
<td></td>
<td>Corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Iopanoic acid</td>
</tr>
<tr>
<td></td>
<td>Propanolol</td>
</tr>
<tr>
<td>Remove excess circulating thyroid hormone</td>
<td>Plasmaphoresis</td>
</tr>
<tr>
<td></td>
<td>Charcoal plasmaperfusion</td>
</tr>
<tr>
<td>Antiadrenergic</td>
<td>Beta blockade</td>
</tr>
<tr>
<td></td>
<td>Reserpine and guanethidine (historical)</td>
</tr>
<tr>
<td>Support systemic decompensation</td>
<td>Hyperthermia: acetaminophen, cooling</td>
</tr>
<tr>
<td></td>
<td>Correct dehydration and nutritional deficits</td>
</tr>
<tr>
<td></td>
<td>Corticosteroids for hypoadrenalism</td>
</tr>
<tr>
<td></td>
<td>Heart failure treatment</td>
</tr>
</tbody>
</table>
+ Thionamide
  - Propylthiouracil, methimazole, carbimazole
  - Inhibit organification and coupling of ioddotyrosines; PTU also inhibit peripheral deiodination of T4 to T3
  - Agranulocytosis occurs in 1:200-500 patients

- Iodine
  - In supraphysiological doses, it initially inhibits thyroid hormone synthesis (Wolff Chaikov effect) and preformed hormone release; onset within 24h
  - Hyperthroid glands then escape from this effect and use iodine as substrate to synthesize more hormones → worsen hyperthyroidism (Jod Basedow effect)
  - Do not give inorganic iodine at least 1 hr after being treated with thionamides

- Beta blockade
  - Use in every patient for control of adrenergic effects (unless contraindicated) - tachycardia, widened pulse pressure, hyperdynamic circulation, anxiety, tremors, muscle weakness, and heat intolerance
  - Propanolol
  - Atenolol, metoprolol and esmolol are also effective
  - At high doses propanolol prevents T4 → T3 conversion (not others)
  - ↑ Metabolism → ↑ dose and dosing frequency
Iopanoic acid
- An oral cholecystographic agent, used in severe thyrotoxicosis requiring rapid control, releases an iodine load when metabolised
- Inhibit hormone synthesis, release and T4 → T3
- Reduce T3 by 6h and 50% by 24h; reduce T4 levels by 24% in 72h
- Production ceased in 2000, not available in Australia

Glucocorticoids
- High doses inhibit T4 → T3
- To treat hypoadrenalism in thyrotoxicosis

Plasmaphoresis and charcoal plasmaperfusion
- Case reports of use in thyroid storm who failed conventional therapies
Rapid preoperative regime for symptom control

- Thionamide
- Beta blockers e.g. propanolol 40mg q6-8h
- High dose glucocorticoids e.g. hydrocortisone 100mg q6h, dex 2mg q8h
- Sodium iopanoate 500mg q6h (not available in Australia)
- Treat for 5 days; but truly emergent cases may still benefit

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drug</th>
<th>Dose</th>
<th>Continue post op?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta blockers</td>
<td>Propanolol</td>
<td>40-80mg PO tds-qid</td>
<td>Continue</td>
</tr>
<tr>
<td></td>
<td>Esmolol</td>
<td>50-100ug/kg/min</td>
<td>Change to oral</td>
</tr>
<tr>
<td>Thionamide</td>
<td>PTU</td>
<td>200mg PO q4h</td>
<td>Stop after total thyroidectomy Continue after nonthyroid surgery</td>
</tr>
<tr>
<td></td>
<td>Methimazole</td>
<td>20mg PO q4h</td>
<td>As above</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Hydrocortisone</td>
<td>100mg PO IV q6h</td>
<td>Taper over 72h</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>2mg PO IV q8h</td>
<td>Taper over 72h</td>
</tr>
</tbody>
</table>
Anaesthesia - Preoperative assessment

- History
  - History of thyroid disease and thyrotoxicosis
  - Mass effect and retrosternal extension

- Examination
  - Signs of thyrotoxicosis
  - Airway assessment, retrosternal extension, SVC obstruction

- Additional investigations
  - Bloods: TFT, EUC, FBC, CMP, LFT, ABG, BSL
  - ECG: sinus tachycardia, ST elevation, QT shortening, AF, ventricular ectopics
  - Echocardiogram
  - Imaging: CXR and lateral thoracic inlet x-ray for tracheal compression
  - Flow volume loop: shows upper airway obstruction in 33%, unrelated to size of goiter
  - CT and MRI: airway anatomy

- Multidisciplinary
  - Endocrine, surgery, ICU
Anaesthesia - Intraoperative

- Monitoring
  - $\text{SpO}_2$, ECG
  - Non-invasive BP and invasive BP
  - BIS/Entropy
  - ETCO$_2$
  - Temperature
  - Neuromuscular blockade monitoring: Facial nerve
  - Consider IDC, CVP, TOE, CO monitoring
  - BSL

- General vs Regional
  - Regional anaesthesia is safe; can decrease sympathetic stimulation from surgical stress; and may be preferred over GA if appropriate

- Premedication recommended
  - Benzodiazepine, narcotic
Prepare for haemodynamic instability and to treat thyroid storm

- Avoid drugs that activate sympathetic system
  - Ketamine, pancuronium, atropine, ephedrine, adrenaline in local anaesthetic, tramadol, pethidine

- Induction
  - Prepare for difficult airway
  - Thiopentone has theoretical advantage over propofol as it inhibits T4→T3 conversion (significance?)
  - Suxamethonium or NDMN blockers except pancuronium
  - Protect the eyes

- Maintenance
  - Adequately depth of anaesthesia to avoid exaggerated sympathetic stimulation
  - No controlled trials on which anaesthetic agent is better
  - Inhalational agents inc. N₂O are safe; no ↑ in MAC
  - ↑ clearance and distribution of propofol, need to ↑ propofol dose in TIVA
  - Opioids are safe, no evidence against fentanyl, morphine or remifentanil
Haemodynamic instability

- Hypertension
  - Beta blockers: continue perioperatively; esmolol infusion intraop, consider using longer acting beta blockers e.g. sotalol
  - Alpha blockers e.g. phentolamine
- Hypotension from ↓ SVR and sympathetic blockade
  - Use direct sympathomimetics e.g. phenylephrine
  - Use fluid
  - Avoid or use very low doses of adrenaline, noradrenaline, dopamine and ephedrine – exaggerated response
  - Avoid atropine – alters heat regulation, causes tachycardia

- ↑drugs and metabolism → higher doses and dosing frequency
- No evidence about dexmedetomidine
Anaesthesia - Postoperative

- Disposition: ICU or HDU

- Analgesia is important
  - Opioids including fentanyl and morphine are safe
  - NSAIDS
    - Avoid aspirin and salicylates inhibit thyroid hormone binding to TBG → can transiently ↑ free T4 and T3
    - Studies show that ibuprofen, naproxen and indomethacin do not alter free or total T4 or T3 levels
    - Cox-2 inhibitors probably safe
    - Avoid ketamine, tramadol

- Continue antithyroid medications and beta blockade

- Supportive management
  - Nutrition, hydration, antipyretial and cooling, BSL management
Complications

- Surgery in poorly controlled thyrotoxicosis has significant postoperative mortality

- Thyroid storm
  - Incidence: rare since the use of the iodine and antithyroid drugs; 1-2%
  - Triggers: infection (commonest trigger), trauma, surgery, anaesthesia, stress, burns, pregnancy and labour, vigorous palpation of thyroid gland, radioactive iodine, iodine contrast, withdrawing antithyroid therapy, aspirin overdose
  - Primarily occur post-operatively in patients not adequately prepared before surgery
  - Pathogenesis is uncertain but to do with sudden increase in free thyroid hormones
  - Diagnosis: clinical; not based on thyroid function tests
  - Table: likelihood of thyroid storm; unlikely <25; impending 25-44; highly likely >45
  - Treatment
    - 1. Antithyroid drugs
    - 2. Block effects of thyroid hormone: beta blocker, corticosteroids for hypoadrenalism, plasmapheresis and plasma exchange can enhance thyroxin clearance
    - 3. Supportive management: hydration, nutrition, electrolyte correction, active cooling and acetaminophen antipyretic
    - 4. Treat underlying trigger
  - If patient survives, T4 and T3 normalize in 24-48h and recover in 1 week
  - High mortality: 20%
  - Case reports of using dantralene in refractory hyperthermia
<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td></td>
<td>HR (bpm)</td>
<td></td>
</tr>
<tr>
<td>37.2-37.7°C</td>
<td>5</td>
<td>90-109</td>
<td>5</td>
</tr>
<tr>
<td>37.8-38.2°C</td>
<td>10</td>
<td>110-119</td>
<td>10</td>
</tr>
<tr>
<td>38.3-38.8°C</td>
<td>15</td>
<td>120-129</td>
<td>15</td>
</tr>
<tr>
<td>38.9-39.3°C</td>
<td>20</td>
<td>130-139</td>
<td>20</td>
</tr>
<tr>
<td>39.4-39.9°C</td>
<td>25</td>
<td>&gt;139</td>
<td>25</td>
</tr>
<tr>
<td>&gt;39.9°C</td>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Mild agitation</td>
<td>10</td>
<td>Mild</td>
<td>5</td>
</tr>
<tr>
<td>Delirium, psychosis, lethargy</td>
<td>20</td>
<td>Moderate</td>
<td>10</td>
</tr>
<tr>
<td>Seizure or coma</td>
<td>30</td>
<td>Severe</td>
<td>15</td>
</tr>
<tr>
<td>GIT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhoea, abdominal pain</td>
<td>10</td>
<td>Present</td>
<td>10</td>
</tr>
<tr>
<td>Unexplained jaundice</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precipitating event</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>10</td>
<td></td>
<td>10</td>
</tr>
</tbody>
</table>
### Differentials of thyroid storm

<table>
<thead>
<tr>
<th></th>
<th>MH</th>
<th>Thyroid storm</th>
<th>Phaeochromocytoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperthermia</td>
<td>Often present</td>
<td>Often present</td>
<td>Maybe present</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Usually present</td>
<td>Usually present</td>
<td>Usually present</td>
</tr>
<tr>
<td>Acidosis</td>
<td>Usually present</td>
<td>May or may not</td>
<td>Maybe present</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Maybe present</td>
<td>Often present</td>
<td>Usually present</td>
</tr>
<tr>
<td>Muscle rigidity</td>
<td>Often present</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>CK</td>
<td>Increased</td>
<td>May or may not</td>
<td>May be increased</td>
</tr>
<tr>
<td>Myoglobinuria</td>
<td>Often Present</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Other</td>
<td>Hyperkalaemia</td>
<td>TFT</td>
<td>VMA, NA, A</td>
</tr>
<tr>
<td>Response to dantrolene</td>
<td>Positive</td>
<td>Doubtful</td>
<td>Maybe dangerous</td>
</tr>
</tbody>
</table>
Cardiac complications
- Tachycardia, hypertension
- Arrhythmia: treat with beta blocker, digoxin
- Angina
- Cardiac failure: high output, congestive cardiac failure

Thyrotoxic periodic paralysis
- Recurrent episodes of paralysis and hypokalaemia in the setting of thyrotoxicosis
- Asian males; 1.8% in Chinese population, 0.1-0.2% in non-Asian
- Disease of skeletal muscle, not nerve or neuromuscular junction; caused by thyroxin induced hypokalaemia
- Affect lower extremities, proximal muscle groups
- Ocular bulbar and respiratory muscles are rarely involved
- Triggered by stress, cold, alcohol, infection, trauma and menses.
- Only occur when thyrotoxic
- Treatment: K replacement, rendering euthyroid, beta blockers

Airway obstruction
Take home message

- May not have enough time to render euthyroid in emergency surgery
  - Start antithyroid treatment
  - Control thyroid hormone effects: beta blockade
  - Supportive is very important

- Anaesthesia
  - Minimise sympathetic stimulation
  - Prepare for haemodynamic instability and cardiovascular complications
  - Prepare to treat thyroid storm

- Multidisciplinary
  - Endocrine, ICU, surgical team
References

- Franklyn J. Thyrotoxicosis. The Lancet 2012, 379; 1155-1166
- Hines RL, Marschall K. Stoelting's Anesthesia and Co-Existing Disease 5th Ed
- Miller RD et al. Miller’s Anaesthesia 7th Ed
- Langley RW. Perioperative management of the thyrotoxic patient. Endocrinol Metab Clin N Am 2003, 32;519-534
- Stathatos N. Thyroid physiology. . Med Clin N Am 2012, 96;165-173
- Varela A. Spinal anesthesia for emergency abdominal surgery in uncontrolled hyperthyroidism. Acta Anaesthesial Scand 2005, 49; 100-13
- Nayak B. Thyrotoxicosis and thyroid storm. Endocrinol Metab Clin N Am 2006, 35; 663-686
- Samuels MH. Variable effects of nonsteroidal anti-inflammatory agents on thyroid function tests. J Clin Endocrinol Metab 2003, 88(12); 5710-5716
- Danzi S. Thyroid hormone and the cardiovascular system. Med Clin N Am 2012, 96;257-268
- Klein I. Thyrotoxicosis and the heart. Endocrinol & Metab Clinics 1998, 27 (1)