

### Perioperative Medicine Summit

Evidence Based Perioperative Medical Care

## Cases in Perioperative Endocrinology

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## Disclosures

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## Objectives

- Managing hypothyroidism in the perioperative setting
- Pre-operative evaluation before adrenal surgery
- Managing hyperthyroidism in the perioperative setting
- Timely recognition and correct management of thyroid storm
- Appropriate dosing of perioperative glucocorticoids

64 year old woman was started on levothyroxine 6 weeks ago for a new diagnosis of hypothyroidism. Which set of repeat thyroid function levels is acceptable to safely undergo semi-urgent surgery?



- A. Free T4 0.5 (0.8-1.6) and TSH 0.2 (0.5-4.5)
- B. Free T4 1.8 (0.8-1.6) and TSH 0.01 (0.5-4.5)
- C. Free T4 0.8 (0.8-1.6) and TSH 34 (0.5-4.5)

- A. Free T4 0.5 (0.8-1.6) and TSH 0.2 (0.5-4.5)

  A low Free T4 and a low TSH is indicative of pituitary failure; the patient almost certainly has co-existing cortisol deficiency
- B. Free T4 1.8 (0.8-1.6) and TSH 0.01 (0.5-4.5) The replacement dose of levothyroxine is excessive, leading to iatrogenic hyperthyroidism
- C. Free T4 0.8 (0.8-1.6) and TSH 34 (0.5-4.5) Mild-moderate hypothyroidism is well tolerated even after open heart surgery

## Perioperative Management of Hypothyroidism

- Patients with hypothyroidism usually tolerate major surgery without much difficulty
- More sensitive to sedatives
- May be slower to wean from ventilator
- May handle free water excretion less well
- •Always check free T4 and TSH during pre-op evaluation of levothyroxine treated patients. (TSH alone is not enough)
- •Emergent surgery can proceed in the face of inadequately treated hypothyroidism.

Ladenson PW, Levin AA, Ridgway EC, et al. Complications of surgery in hypothyroid patients. Am J Med 1984;77:261–6.

## Perioperative Management of Hypothyroidism

- The half-life of levothyroxine is 7 days
- If enteral dosing (PO or tube feed) of levothyroxine can be resumed within 3-5 days after surgery, free T4 levels will remain in a reasonable range.
- If enteral absorption will not be available for a longer period of time, then best to replace with IV levothyroxine.
- PO levothyroxine tablets are  $\sim$  80% absorbed, thus a maintainence dose of IV levothyroxine can be reduced by 20% as compared with a previous baseline oral daily dose
- IV levothyroxine goes on/off national shortage, it can be withheld if Free T4 and TSH are normal

- The endocrinology consult service was called to see a patient in the SICU. She was a 33 year old woman who had developed hypotension after undergoing left adrenalectomy earlier that day.
- •She had a h/o Neurofibromatosis type 1 complicated by the development of multiple high grade malignant peripheral nerve sheath tumors. She had undergone chemotherapy and previous surgical resections.
- •In the course of her follow-up a left adrenal mass was noted which was slowly growing and was described on CT as "concerning for metastatic disease".

- Her only other past medical history was primary hypothyroidism treated with levothyroxine 200 mcg/day
- •During the operation her BP was highly labile with episodes of hypertension requiring IV nitroglycerin alternating with hypotension
- •In the evening of POD 0 she developed lactic acidosis and was started on IV norepinephrine and stress doses of hydrocortisone.
- •We were asked to see her concerning possible adrenal crisis/glucocorticoid deficiency.

- Exam revealed a groggy post-op patient, extubated, with BP 100/70 and HR 116 on IV pressors and IV steroids. Multiple neurofibromas were present diffusely and a café au lait spot was on her right neck
- •She had no history of hypertension and BP had been normal during multiple visits for chemotherapy in the past several months
- Free T4, TSH, CBC, CMP had been checked preoperatively and were all normal.

- She stabilized over the next several days but then had several episodes of dropping hemoglobin. Abdominal CT revealed new areas of splenic and renal infarction. She developed hemorrhagic ascites requiring paracentesis
- After 2 weeks in the SICU she made a slow recovery and was discharged home

•What was the pathology of the left adrenal mass?

## Pheochromocytoma

#### Neurofibromatosis type 1

- Multiple cutaneous neurofibomas
- •Brown pigmented areas of skin (café au lait) with smooth borders "coast of california"
- Peripheral nerve sheath tumors
- Skeletal dysplasisas
- Pheochromocytoma in 1-5% of patients with NF-1

#### Pre-operative Diagnosis of Pheochromocytoma

- All adrenal masses are suspected to be pheochromocytoma until proven otherwise.
- 10% of pheochromocytoma are extra-adrenal, almost all are para-aortic within the abdomen known as paragangliomas
- Although most patients with pheochromocytoma have sustained or paroxysmal hypertension, some do not
- In the radiologic diagnosis of adrenal masses, benign cortical tumors have a typical low density, while adrenal cancer, adrenal metastasis, and pheochromocytoma all have high density and will look alike.

#### Pre-operative Diagnosis of Pheochromocytoma

- It is always important to identify pheochromocytoma prior to surgical resection in order to prepare the patient with alpha blockade for 4-6 weeks prior to resection.
- Patients who undergo surgery without adequate preparation will typically undergo circulatory crisis and collapse
- The same logic applies to biopsy of the adrenal mass. Never stick a needle into an adrenal mass until pheochromocytoma has been ruled out.
- Diagnosis of pheochromocytoma requires a high index of suspicion and generally one blood test
- •Plasma Metanephrines is a highly reliable tool, and 24 hr urine collections are generally not needed.

## Perioperative Management of Hyperthyroidism

- Always include Free T4 and TSH levels in pre-op assessment of all patients with any h/o thyroid disease
- No patient with an elevated Free T4 and a non-detectable TSH should be cleared for elective surgery. This includes hypothyroid patients who are excessively over-replaced.
- All patients with un-controlled hyperthyroidism must be rendered euthyroid before all surgery unless extremely emergent. This will generally take 4 weeks.
- A hyperthyroid patients who must have emergent surgery should be emperically treated for thyroid storm.

### Perioperative Management of Hyperthyroidism

- Amiodarone induced hyperthyroidism
  - Treated with methimazole and/or steroids
  - •Stopping amiodarone requires 3-4 months for a benefit. Some patients can't be stopped
  - •Total thyroidectomy may be the only viable option.
  - •Patients with severe amio-induced hyperthyroidism typically tolerate thyroidectomy very well.
  - •Amiodarone has strong beta-blocking properties so that tachycardia is not usually an issue

### A case of Acute Appendicitis

- 28 year old woman presented to the emergency ward complaining of abdominal pain, vomiting, and dyspnea.
- Temp was 101.4, BP 100/70, HR 132, RR 24
- RLQ tenderness was present and CT confirmed the diagnosis of acute appendicitis.
- She gave a history of hyperthyroidism diagnosed 12 months ago but ran out of methimazole 8 months ago and had been lost to follow up.
- After consultation between surgery and anesthesia, she was given propranolol 1 mg IV followed by a second mg IV.

### A case of Acute Appendicitis

- WBC was 17.6, CMP was normal
- ECG: sinus tachycardia rate 142
- There was no response of the elevated heart rate to IV propranolol. HR continued 135-150 on cardiac monitor
- She was taken to the OR for emergent appendectomy
- The inflammed unruptured appendix was removed and after recovery she was admitted to the general surgical unit
- Her vital signs remained the same and propranolol 20 mg PO q6 hours was begun.
- Two hours later she became dyspneic and hypoxic.

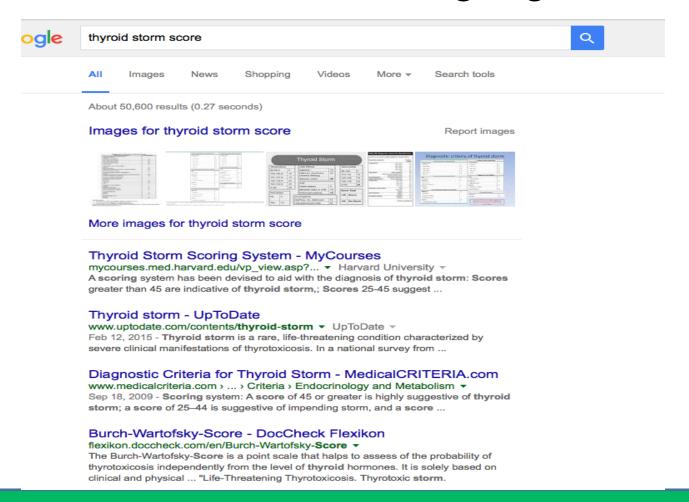
## A case of Acute Appendicitis

- BP dropped from 100 sys into the 80's
- •HR continued 135-150 on cardiac monitor
- She was transferred to the ICU and given IV fluid boluses and oxygen by mask
- Acutely she became more hypotensive, her heart rate dropped into the 70's and she had a respiratory arrest
- Despite intubation she was unable to be stabilized and after unsucessful recusitation, she died.
- Autopsy showed histological changes of her thyroid typical of Graves' disease but was otherwise unremarkable.

# Diagnosing Thyroid Storm You Need To Know the Score

Criteria	Points	Criteria	Points	
Thermoregulatory dysfunction		Gastrointestinal-hepatic dysfunction		
Temperature (°F)		Manifestation		
99.0-99.9	5	Absent	0	
100.0-100.9	10	Moderate (diarrhea, abdominal pain, nausea/vomiting)	10	
101.0-101.9	15	Severe (jaundice)	20	
102.0-102.9	20			
103.0-103.9	25			
≥ 104.0	30			
Cardiovascular		Central nervous system disturbance		
Tachycardia (beats per minute)		Manifestation		
100-109	5	Absent	0	
110-119	10	Mild (agitation)	10	
120-129	15	Moderate (delirium, psychosis, extreme lethargy)	20	
130-139	20	Severe (seizure, coma)		
> 140	25	server (server) sommy		
Atrial fibrillation				
Absent	0			
Present	10			
Congestive heart failure	100	Precipitant history		
Absent	0	Status		
Mild	5	Positive	0 13	
Moderate	10	Negative	10	
Severe	20			
Scores totaled				
> 45	Thyroid storm			
25-44	Impending storm			
<25	Storm unlikely			

# Don't try to remember the scoring system Just remember to google



# Diagnosing Thyroid Storm Our Patient

• Temperature 101.4 15 points

Tachycardia 136 20 points

Atrial fibrillation 0 points

Heart Failure (mild) 5 points

GI-hepatic dysfunction 0 points or 10 for vomiting?

CNS disturbance
 0 points

Precipitating cause 10 points

total: 50 points

(<25 = no storm, 25-45 = impending storm, > 45 = in thyroid storm

## Treatment of Thyroid Storm

- Immediate ICU care is a must
- Treat the precipitant, don't aggravate it
- IV esmolol infusion, titrate rapidly to a safe HR
- Tylenol, cooling blankets for high fever
- Prophylthiouracil, high dose every 6 hours
- IV stress dose glucocorticoids
- Super saturated potassium iodine
- Treat heart failure or hypovolemia as needed

Which patient needs 100 mg of IV hydrocortisone in the pre-op holding area?



A. Has taken prednisone 40 mg QAM for 3 mo

B. Has taken prednisone 5 mg QAM for 5 yrs

C. Takes dexamethasone 10 mg for two days every 3 weeks as part of chemotherapy

- A. Prednisone 40 mg QAM for 3 mo will cause profound suppression of the HPA axis and perioperative hydrocortisone is a must.
- B. Prednisone 5 mg QAM for 5 yrs will not cause suppression of the HPA axis. The replacement dose of prednisone is 6 mg daily and so lower doses are not suppressive.
- C. Dexamethasone 10 mg for two days every 3 weeks also will not suppress the HPA axis. Suppression will begin to occur after continuous therapy for 7 days or more.

### Perioperative management of glucocorticoids

- Chronic therapy with prednisone doses greater than 6-7 mg/day for more than 2-3 weeks will cause suppression of the HPA axis and all such patients should receive 100 mg IV hydrocortisone in the pre-op holding area
- Dexamethasone is more suppressive than prednisone given QAM (longer half-lfe)
- Post-op IV hydrocortisone 50 mg every 8 hrs is recommended until oral baseline therapy is appropriate

## The Rush Steroid Card

e GI	uco	cortico	id Repla	cement	(mg)
1	P	AM	Noon	PM	Total
V	0				Day
	*	25	_	12.5	37.5
*	*	0.75	-	-	0.75
*	*	10	5	5	20
*	*	3		2	5
	1	I P V O	I P AM V O * 25  * * 0.75  * * 10	I P AM Noon V O * 25  * * 0.75  * * 10 5	V O       * 25       * * 0.75       * * 10       5

#### The Rush Steroid Card

All patients with primary or secondary adrenal insufficiency including all patients on chronic daily glucocorticoids

Stress	Glucocorticoid Dosing		
Mild	Hydrocortisone 25 mg or equiv IV q 8 h		
Moderate	Hydrocortisone 50 mg or equiv IV q 8 h		
Severe	Hydrocortisone 100 mg or equiv IV q 8 h		
Perioperative	Hydrocortisone 100 mg or equiv IV q 8 h Pre-op, 2 hours pre-op, then 50 mg IV q 8 hours post-op		

Preventing postoperative nausea and vomiting Is perioperative dexamethasone a good idea?

- Post-op nausea or vomiting is reported to affect 80% of patients after general anesthesia
- A recent Cochrane analysis finds that if all patients are given an anti-emetic during surgery, 28% will benefit and 72% will not.
- Dexamethasone 4-8 mg RR 0.51 vs placebo
- Ondansetron 4 mg RR 0.55 vs placebo
- Dexamethasone may also reduce post pain and reduce opioid requirements (less data)

Drugs for preventing postoperative nausea and vomiting (Review) Copyright © 2014 The Cochrane Collaboration.

# Dexamethasone for Prevention of Postoperative nausea and vomiting

- The major side-effect is to cause postoperative hyperglycemia for 6-24 hours in susceptible hosts
- Non-diabetic women 20% had blood glucose > 153
- Obese non-diabetic patients: mean blood glucose 187
- Diabetic patients: mean blood glucose 157
- Multivariate analysis in a recent case-control study found the risk of postoperative infection to be increased 3-fold after dexamethasone as compared with no dexamethasone
- Other studies have shown positive and negative associations

Anaesth Intensive Care 2010; **38:** 661-666 Consensus Guidelines for the Management of Postoperative Nausea and Vomiting, Anesth Analg 2014;118:85–113)

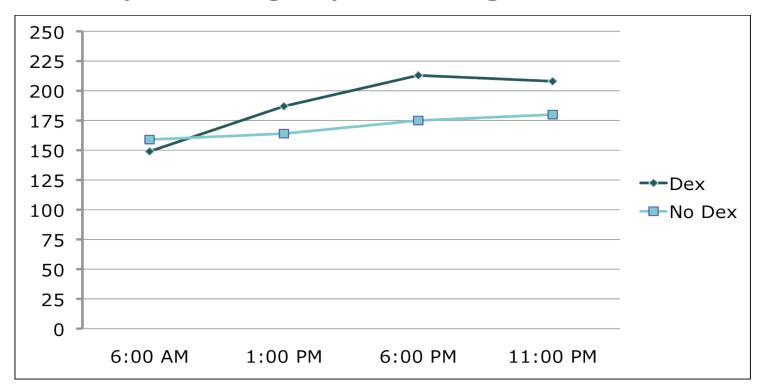
# Dexamethasone for Prevention of Postoperative nausea and vomiting

- At Rush the endocrinology inpatient diabetes team see all postoperative patients with diabetes
- All patients with diabetes are identified in real time as they arrive on their general surgical units
- We begin Q 6-hourly monitoring of blood glucose in all patients with diabetes immediately after surgery
- We begin SQ insulin management in all patients with blood glucose >
   160 mg/dl as soon as they reach the general surgical units
- The typical patient will begin subcutaneous insulin glargine 0.2-0.3 units/kg on the night of surgery.
- Correction doses of insulin lispro are added for blood glucose levels greater than 180-200 mg/dl

### Rush study of postoperative hyperglycemia

	No dexamethasone	dexamethasone
Number	100	100
Mean age (years)	66±11	63±11
Female sex	61 %	60 %
Type of surgery		
Orthopedic	79 %	72 %
Gyne	14 %	20%
General surgery	7 %	8 %
Dose of intra-op		
dexamethasone		
4-6 mg	0	55 %
8-12 mg	0	45 %
Mean HBA1C	7.3 ± 1.2%	7.4 ± 1.6
Pre-operative therapy		
metformin	61 %	69 %
sulfonylurea	41 %	39 %
other orals	39 %	62 %
insulin	40 %	36 %
Mean length of stay	3.8 days	3.6 days

## Rush study of postoperative hyperglycemia Day of surgery blood glucose levels



In the first 24 hours after surgery, dex-treated patients received a mean of 30 units of insulin, vs 19 units of insulin for non-dex patients (p<0.01)

# What conclusions can we draw about dexamethasone and postoperative hyperglycemia?

- A multicenter randomized clinical trial is needed to assess if hyperglycemia and/or other effects of dexamethasone given to patients with diabetes will lead to postoperative adverse effects especially infections.
- 2. For now should perioperative dexamethasone be avoided in patients with known diabetes?
- 3. Should ondansetron be preferred in patients with known diabetes?

# Treatment of dexamethasone aggravated postoperative hyperglycemia?

Clinicians who manage postoperative hyperglycemia should be aware that dexamethasone increases post-op blood glucose levels in most patients with type 2 diabetes

- Substantial increases in the first post-op doses of basal and correction insulin will be required
  - 0.3-0.4 units/kg basal insulin
  - 0.1-0.15 units/kg correction rapid-acting insulin
- 24 hours later insulin doses will need to be reduced and re-titrated

Thank-you

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