Pituitary
Pituitary

- 44 yo female est. care
- 8 yrs ago, diagnosed with “prolactinoma”
  - Prolactin 120 ng/ml (4-30 ng/ml)
  - MRI 6 mm microadenoma
- Rx with bromocriptine then cabergoline
- Dose escalated to cabergoline 1.5 mg 2x/week
- Menstrual irregularities, trying to conceive
Pituitary

• Labs:
  – Pregnancy test: negative
  – Prolactin: 84 ng/ml (4-30)
  – LH: 2 mIU/ml (1-18)
  – FSH 3 mIU/ml (2-12)
  – IGF-1: 355 ng/ml (113-297)
  – FT4: 1.0 ng/ml (0.9-1.8)

• MRI: 11 mm pituitary lesion (from 6 mm)
Pituitary

• What would you recommend:
  a. Referral to reproductive endocrinologist for fertility treatments
  b. Increase cabergoline to 4 mg weekly
  c. Gamma-knife
  d. Transphenoidal surgery
Pituitary- Things need to know

- Pituitary adenoma- 10-30% prevalence
- Most common tumor: non-functioning
- Most common functioning: prolactinoma
Things to know about Prolactinoma

• **Tumor size correlates with prolactin level**
  – Microadenoma: < 200 ng/ml
    ● 6 mm: 120 ng/ml
  – Macroadenoma (1-2cm): 200-1000 ng/ml
  – > 2cm: >1000 ng/ml
Pituitary
CLINICAL PEARLS

• Tumor size correlates with level
  – Microadenoma: < 200 ng/ml
    • 6 mm: 120 ng/ml
  – Tumor 1-2cm: 200-1000 ng/ml
  – > 2cm: >1000 ng/ml
  – Pituitary Stalk Compression: <150 ng/ml
  – Treatment is Dopamine agonists
    • Drop in both cases: can’t distinguish between stalk compression vs. prolactinoma
Pituitary

• Our patient:
  – 6 mm: 120 ng/ml
  – 11 mm: 84 ng/ml

• Causes:
  – 10% resistance to dopamine agonists
    • Intolerance to drug, variation in receptor expression
  – Dual secretor: GH/prolactin
    • IGF-1: 355 ng/ml (113-297)
Pituitary

• What would you recommend:
  a. Referral to reproductive endocrinologist for fertility treatments
  b. Increase cabergoline to 4 mg weekly
  c. Gamma-knife radiation
  d. Transphenoidal surgery
Pituitary

- 44 yo female est. care
Guinness Records

70 Year-old Indian Woman Welcomes First Baby

by Lisa Arneill in Premature Babies, Rajo Devi, World’s Oldest Mom

An Indian woman, Rajo Devi, gave birth to a child at the age of 70 in December 2008. This event was recorded in the Guinness World Records for being the oldest woman to give birth.
Guinness Records

66 Year-Old Indian Woman Welcomes Triplets

By Lisa Arneill on 15 Jun, 2010 in Multiple Births, pregnancy

A childless Indian woman has become the oldest person in the world to have triplets – at the unbelievable age of 66.

Bhateri Devi and her husband Deva Singh, 64, are celebrating their arrival of their first, second and third babies nearly 44 years after
Pituitary

• What would you recommend:
  a. Referral to reproductive endocrinologist for fertility treatments
  b. Increase cabergoline to 4 mg weekly
  c. Gamma-knife
  d. Transphenoidal surgery
Take Home Points

• If something didn’t respond as expected, take a step back to reevaluate

• Clinical Pearls: Size matters!
QUESTIONS?
Parathyroid
Parathyroid

- Calcium: 10.4 (8.2-10.2)
- PTH: 80 (10-65)
- Vitamin D: 26 (30-100)

- Albumin: 4.0
- Phosphorus: 2.8
- Urinary calcium: 300 mg/24 hr (100-250 mg/24 hr)
- Urinary Creatinine: 1gm/24 hr
CLINICAL PEARLS

• Strong **INVERSE CORRELATION** between pth and calcium
  – Low calcium, high pth
  – High calcium, low pth
Parathyroid

• Calcium: 10.4 (8.2-10.2)
• PTH: 80 (10-65)
• Vitamin D: 26 (30-100)

PRIMARY HYPERPARATHYROIDISM
Parathyroidism

- PTH is “INAPPROPRIATELY NORMAL” in the setting of hypercalcemia
  - Calcium 10.4 (<10.2), PTH 50 (10-65)
- Occur in 15-20% of all primary hyperparathyroidism cases
- Main clue: Worst DXA values at WRIST
Cancellous or Trabecular

Compact Bone & Spongy (Cancellous Bone)

- Lacunae containing osteocytes
- Lamellae
- Canaliculi
- Osteon of compact bone
- Trabeculae of spongy bone
- Haversian canal
- Periosteum
- Volkmann's canal
Densitometric Signature of Primary Hyperparathyroidism

Silverberg et al. JBMR, 1989
Parathyroid

• Workup:
  – History: bones, stones, abdominal moans, and psychological overtones
  – DXA (wrist)
  – 24 hr urinary calcium with Cr.
  – Sestamibi scan +/- parathyroid Ultrasound
  – CT angiogram of parathyroid
  – 4-D CT with SPECT imaging
  – MRI
Imaging Pearls

• Imaging has **no utility in confirming or excluding** the diagnosis of pHPT.
• Imaging results should not be used to select patients for surgical referral. Patients with **negative imaging results remain candidates** for parathyroidectomy.
• There is marked regional variability in imaging accuracy. When imaging with initially negative results is performed again at high-volume centers, the sensitivity of localization improves to as high as 92%
• If patient doesn’t want surgery- **DON’T DO imaging**.
• Patients who are candidates for surgery and have negative or discordant imaging results should still be referred to a parathyroid surgeon for evaluation.
Without Parathyroid Surgery 15-Year Course of BMD
Indications for Surgery in Asymptomatic Primary Hyperparathyroidism

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum calcium (above normal)</td>
<td>&gt; 1.0 mg/dL</td>
</tr>
<tr>
<td>Renal Involvement (silent stones) with Creatinine Clearance</td>
<td>If &lt; 60 cc/min</td>
</tr>
<tr>
<td>Hypercalciuria</td>
<td>24-hr urine calcium level &gt;400 mg/dL</td>
</tr>
<tr>
<td>Bone density</td>
<td>T-score &lt; -2.5 at any site or fragility Fx</td>
</tr>
<tr>
<td>Age</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Compliance</td>
<td>Unwilling to comply with observation protocols</td>
</tr>
</tbody>
</table>
Concurrent Thyroidectomy

• In patients with pHPT, concomitant thyroid disease is frequent (12%-67%)
• Patients undergoing parathyroidectomy should have preoperative thyroid evaluation because of the high rate of concomitant disease, which may require thyroid resection
• The indications for thyroidectomy for concomitant thyroid disease during parathyroidectomy for pHPT are the same as those for patients with isolated thyroid disease and should follow evidence-based guidelines
• Endocrinology referral- appropriate
Clinical Pearls

• Strong correlation between PTH level and calcium concentration, just because there is no “H” or “L” next to the lab doesn’t mean it’s normal.

• Always think about primary hyperparathyroidism when wrist DXA value is out of proportion to the rest of the DXA scan

• If surgery is indicated, evaluate thyroid also
QUESTIONS?
Thyroid
Thyroid nodules

- Thyroid nodules are common - up to 50%
- Risk of carcinoma: approx. 5% for EACH nodule
- Presence of multiple nodules does not lower the risk of cancer
Clinical Pearls

• First test to order when encountered with a thyroid nodule is: TSH

• **DO NOT** order a THYROID UPTAKE AND SCAN unless the TSH is **LOW**

• Thyroid uptake and scan is only useful when you are hyperthyroid
Devil’s Advocate

• What about cold nodule?

• RAIU only useful to rule out HOT nodules
  – Risk of cancer essentially 0%
  – Cold nodule CA risk: 15-20%
Summary

• If the serum TSH concentration is low, indicating overt or subclinical hyperthyroidism, thyroid scintigraphy should be performed next

• If the serum TSH concentration is normal or elevated, NO RAIU is needed
Thyroid Nodule Algorithm

1. **Patient with thyroid nodule**
2. **TSH**
   - **Normal or elevated TSH**
     - Ultrasound to assess need for biopsy
       - Do not meet criteria
         - Monitor with serial US
       - Meet criteria
         - Fine needle aspiration
   - **Suppressed TSH**
     - Cold nodule
     - **RAI scan**
       - Hot nodule
     - Treatment for hyperthyroidism
Thyroid Ultrasound
Ultrasound
Fine Needle Aspiration
U/S Guided Fine Needle Aspiration
Cold left nodule
Thyroid Uptake and Scan

- DON’T BIOPSY hot nodules
Thyroid nodules PEARLS

- Not all thyroid nodules need to be biopsied
- First thing to do if there are thyroid nodules is NOT to order a biopsy-remember the workup

- Endocrinology Referral
Treatment Options

- Antithyroid Drugs
- I-131 ablation
- Surgery
Anti-Thyroid Drugs

- Methimazole (Tapazole)
  - Dosed 10-30 mg daily or bid
  - Advantages: longer half-life, shorter time to normalization, less effect on liver

- PTU (propylthiouracil)
  - Black box warning for liver toxicity
  - 100 mg tid starting dose
  - Use for pregnancy
CLINICAL PEARLS

• Methimazole is the drug of choice to treat hyperthyroidism
• 1\textsuperscript{st} trimester of pregnancy- PTU
Aplasia Cutis Defect
Esophageal Aphasia

(A) Normal anatomy of baby's esophagus and trachea. (B) During prenatal development, a baby's upper digestive tract may form abnormal gaps and connections. (C) These birth defects are known as esophageal atresia and tracheoesophageal fistula.
Surgery for TEF/EA involves a small incision (left). The surgeon then closes the fistula and repairs the baby’s esophagus (center) and trachea (right).
Choanal Atresia is a condition in which the back of the nasal passage is blocked by bone or soft tissue. Some babies have a blocked nasal passage on one side.
Choanal Atresia

Footnote: (A) Unilateral choanal atresia; (B) Bilateral choanal atresia.
• 32 cases of serious liver injury for PTU
  – 12 deaths, 5 liver transplants
  – Pediatric: 1 death, 6 liver transplants

• 5 cases of serious liver injury with MMI
  – 3 deaths, all adults
RECOMMENDATION 13
Methimazole should be used in virtually every patient who chooses antithyroid drug therapy for GD, except during the first trimester of pregnancy when propylthiouracil is preferred, in the treatment of thyroid storm, and in patients with minor reactions to methimazole who refuse radioactive iodine therapy or surgery. 1/++0

RECOMMENDATION 51
Methimazole should be used in virtually every child who is treated with antithyroid drug therapy. 1/++0
Hyperthyroidism

- Patient on MMI should switched to PTU at first positive pregnancy test
- After first trimester, switch back to MMI
- If first trimester already passed, start MMI, NOT PTU
- MMI 30x more potent on mg-mg basis, so 300 mg PTU is roughly equivalent to 10 mg MMI
Hyperthyroidism

- Both MMI and PTU crosses placenta
- Due to toxicity of PTU, MMI is preferred drug on nursing women
Hyperthyroid Summary

• MMI in all adults, children, pregnant women in 2\textsuperscript{nd} and 3\textsuperscript{rd} trimester, as well as nursing women

• PTU should only be used in 1\textsuperscript{st} trimester of pregnancy
  – ATA, TES, AACE, FDA
QUESTIONS?
Hypothyroidism

- Fatigue
- Weight gain
- Dry skin and cold intolerance
- Yellowing or yellow hue of the skin
- Coarseness or loss of hair
- Hoarseness
- Goiter
- Delayed relaxation of deep tendon reflexes
- Ataxia

- Constipation
- Memory and mental impairment
- Decreased concentration
- Depression
- Irregular or heavy menses and infertility
- Myalgias
- Hyperlipidemia
- Bradycardia and hypothermia
- Myxedema

Overlapping Symptoms

Depression
- Sleep decrease
- Suicidal ideation
- Weight loss
- Appetite increase/decrease

Hypothyroidism
- Constipation
- Appetite decrease
- Decreased concentration
- Decreased libido
- Delusions
- Depressed mood
- Diminished interest
- Sleep increase
- Weight increase
- Fatigue

Bradycardia
- Cardiac and lipid abnormalities
- Cold intolerance
- Delayed reflexes
- Goiter
- Hair and skin changes

All these years, it's been my thyroid?!
YOU DON'T UNDERSTAND, I HAVE A THYROID PROBLEM

BECAUSE OF ALL THE FOOD I EAT
Hypothyroidism

• Current TSH reference range is too wide

• “My chiropractor said my TSH is 3 and it should be less than 1. Can I have more thyroid medication please.”
The Wolff-Chaikoff Effect. Panel A shows a proposed mechanism of the acute Wolff-Chaikoff effect. During the first day of iodine exposure, the sodium-iodide symporter transports the excess iodine into the thyroid, resulting in transient inhibition of thyroid peroxidase (TPO) and a decrease in thyroid hormone synthesis. Panel B shows the mechanism that turns off the acute Wolff-Chaikoff effect: a dramatic decrease in sodium-iodide symporter expression results in decreased iodine transport and the subsequent resumption of thyroid hormone synthesis. DIT denotes diiodothyrosine, I iodide, MIT moniodothyrosine, T3 triiodothyronine, and T4 thyroxine. Reprinted from P. Pramyothin et al. Clinical problem-solving: A hidden solution. N Engl J Med. 2011;365:2123–2127 (26), with permission. ©
Many Patients With Hypothyroidism Report no Symptoms
Hypothyroidism PEARLS

- Check **TPO antibodies** in hypothyroid patients
- If TPO antibodies is positive, treat the patient to bring TSH < 2
- If TPO abs is negative, lowering TSH will not make a difference
Hypothyroidism- TPO abs

- **Women** who are TPO abs POSITIVE have a higher incidence of miscarriage
- All women of child-bearing age with family history of thyroid disease should be tested for TPO abs.
- If POSITIVE, treat to keep TSH to < 2
Significantly Increased Risk of Miscarriage in Women That Are TPO (+) vs. TPO (-)

Best Practice & Research Clinical Endocrinology & Metabolism 2004;18:167-181
BRAND NAME VS. GENERIC
FDA Requirements for Bioequivalence

- Product A is bioequivalent to the reference drug; its 90% confidence interval of the AUC falls within 80% to 125% of the reference drug.
- Product B is not bioequivalent to the reference drug; its 90% confidence interval of the AUC falls outside of 80% to 125% of the reference drug.

Narrow Therapeutic Range

• Current FDA bioequivalence and therapeutic equivalent evaluation guidelines may not be appropriate for assessment of narrow therapeutic range drugs

• A 20%-25% potential difference in bioavailability would alter therapeutic effects
TSH Change Following a Change in LT4 Product

![Bar chart showing TSH change following a change in LT4 product.](image-url)

- Patients ≤0.5: 33.2%
- Patients >0.5-1.0: 19.9%
- Patients >1.0-1.5: 16.8%
- Patients >1.5-2.0: 5.1%
- Patients >2.0: 25%

Medical Letter

• “Given the multiple sources of variation in the effects of a dose of the drug, there is no good reason to introduce another one by substituting a generic that could be switched without prescriber’s knowledge from one refill to the next.”

Clinical Pearls

• Pick one brand and stick with it. Do not allow generic substitution

• Confirm the LT4 brand the patient is taking at each visit
  • ATA, TES, AACE recommendations.
QUESTIONS?
Diabetes UPDATES
GLYCEMIC CONTROL ALGORITHM

**INDIVIDUALIZE GOALS**

- **A1C ≤6.5%** For patients without concurrent serious illness and at low hypoglycemic risk
- **A1C >6.5%** For patients with concurrent serious illness and at risk for hypoglycemia

**LIFESTYLE THERAPY AND ONGOING GLUCOSE MONITORING** (CGM preferred)

- Independent of glycemic control, if established or high ASCVD risk and/or CKD, recommend SGLT2i and/or LA GLP1-RA

**Entry A1C ≥7.5% - 9.0%**

- **DUAL THERAPY**
  - GLP1-RA
  - SGLT2i
  - DPP4i
  - TZD
  - SU/GLN
  - Basal Insulin
  - Colesevelam
  - Bromocriptine QR
  - AGi

- **TRIPLE THERAPY**
  - GLP1-RA
  - SGLT2i
  - TZD
  - SU/GLN
  - Basal Insulin
  - DPP4i
  - Colesevelam
  - Bromocriptine QR
  - AGi

**Entry A1C >9.0%**

- **SYMPTOMS**
  - **NO**
    - DUAL Therapy
    - OR
    - TRIPEL Therapy
  - **YES**
    - INSULIN ± Other Agents

ADD OR INTENSIFY INSULIN
Refer to Insulin Algorithm

**LEGEND**
- Few adverse events and/or possible benefits
- Use with caution

---

**MONOTHERAPY**

- Metformin
- GLP1-RA
- SGLT2i
- DPP4i
- TZD
- AGi
- SU/GLN

**Entry A1C <7.5%**

- Independent of glycemic control, if established ASCVD or high risk, CKD 3, or HFrEF, start LA GLP1-RA or SGLT2i with proven efficacy

---

**PROGRESSION OF DISEASE**

1. Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation
2. If not at goal in 3 months, proceed to next level therapy

*CKD 3: canagliflozin; HFrEF: dapagliflozin
CKD 3 = stage 3 chronic kidney disease; HFrEF = heart failure with reduced ejection fraction; LA = long-acting (24 hour duration)
CVOTs showing positive CV outcomes have been acknowledged in clinical recommendations

CVOT data release and first acknowledgment by major societies

<table>
<thead>
<tr>
<th>Year</th>
<th>Data release</th>
<th>Diabetes</th>
<th>CV disease</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>EMPA-REG OUTCOME®1 Empagliflozin</td>
<td>Empagliflozin Feb 20167</td>
<td></td>
<td>Empagliflozin May 20167</td>
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<tr>
<td>2016</td>
<td>LEADER®2 Liraglutide</td>
<td>Liraglutide Sep 20168</td>
<td></td>
<td></td>
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<tr>
<td>2017</td>
<td>SUSTAIN-6®3 Semaglutide</td>
<td>Liraglutide Jan 20179</td>
<td>Four CVOTs* Oct 201710</td>
<td>Empagliflozin August 201718</td>
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<tr>
<td>2018</td>
<td>CANVAS Program®4 Canagliflozin</td>
<td></td>
<td>Semaglutide &amp; canagliflozin Jan 201811</td>
<td>Canagliflozin March 201819</td>
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<tr>
<td></td>
<td>Harmony Outcomes®5 Albiglutide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>DECLARE-TIMI 58®6 Dapagliflozin</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*EMPA-REG OUTCOME®, LEADER, SUSTAIN-6 and CANVAS Program; †EMPA-REG OUTCOME®, LEADER, SUSTAIN-6, CANVAS Program and HARMONY Outcomes
CVOT, cardiovascular outcomes trial
See slide notes for full list of references
Evidence from CVOTs has shown that SGLT2 inhibitors and GLP-1 RAs have beneficial effects on CV outcomes

<table>
<thead>
<tr>
<th>EMPA-REG OUTCOME¹ (empagliflozin)</th>
<th>CANVAS Program²,³ (canagliflozin)</th>
<th>DECLARE-TIMI 58⁴ (dapagliflozin)</th>
<th>LEADER⁵ (liraglutide)</th>
<th>SUSTAIN-6⁶ (semaglutide)</th>
<th>Harmony Outcomes⁷ (albiglutide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3P-MACE</td>
<td>HR 0.86 (95% CI 0.74, 0.99)</td>
<td>HR 0.86 (95% CI 0.75, 0.97)</td>
<td>HR 0.93 (95% CI 0.84, 1.03)</td>
<td>HR 0.87 (95% CI 0.78, 0.97)</td>
<td>HR 0.74 (95% CI 0.58, 0.95)</td>
</tr>
<tr>
<td>CV death</td>
<td>HR 0.62 (95% CI 0.49, 0.77)</td>
<td>HR 0.87 (95% CI 0.72, 1.06)</td>
<td>HR 0.98 (95% CI 0.82, 1.17)</td>
<td>HR 0.78 (95% CI 0.66, 0.93)</td>
<td>HR 0.93 (95% CI 0.73, 1.19)</td>
</tr>
<tr>
<td>HHF</td>
<td>HR 0.65 (95% CI 0.50, 0.85)</td>
<td>HR 0.67 (95% CI 0.52, 0.87)</td>
<td>HR 0.73 (95% CI 0.61, 0.88)</td>
<td>HR 0.87 (95% CI 0.73, 1.05)</td>
<td>HR 1.11 (95% CI 0.77, 1.61)</td>
</tr>
<tr>
<td>CV death or HHF</td>
<td>HR 0.66 (95% CI 0.55, 0.79)</td>
<td>HR 0.78 (95% CI 0.67, 0.91)</td>
<td>HR 0.83 (95% CI 0.73, 0.95)</td>
<td>HR 0.87 (95% CI 0.73, 1.05)</td>
<td>HR 0.85 (95% CI 0.70, 1.04)</td>
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<tr>
<td>Non-fatal stroke</td>
<td>HR 1.24 (95% CI 0.92, 1.67)</td>
<td>HR 0.90 (95% CI 0.71, 1.15)</td>
<td>HR 1.01 (95% CI 0.84, 1.21)</td>
<td>HR 0.89 (95% CI 0.72, 1.11)</td>
<td>HR 0.61 (95% CI 0.38, 0.99)</td>
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<tr>
<td>Fatal/non-fatal MI</td>
<td>HR 0.87 (95% CI 0.70, 1.09)</td>
<td>HR 0.89 (95% CI 0.73, 1.09)</td>
<td>HR 0.89 (95% CI 0.77, 1.01)</td>
<td>HR 0.88 (95% CI 0.75, 1.03)</td>
<td>HR 0.74 (95% CI 0.51, 1.08)</td>
</tr>
</tbody>
</table>

Comparison of studies should be interpreted with caution due to differences in study design, populations and methodology.

*p-values are for superiority.
*Nominal p-value; †Testing for superiority for 3P-MACE was part of the statistical analysis plan, but was not part of the hierarchical testing strategy.
‡Exploratory outcome, no p-value is reported – only nominal effect estimate is given; §Testing for superiority was neither prespecified nor adjusted for multiplicity.
HFF, hospitalisation for heart failure; NR, not reported.

### CV Outcomes of SGLT2 Inhibitors

<table>
<thead>
<tr>
<th>Study</th>
<th>MACE</th>
<th>CV Death</th>
<th>HHF</th>
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<tbody>
<tr>
<td>EMPA-REG OUTCOME[a]</td>
<td>0.86</td>
<td>0.62</td>
<td>0.65</td>
</tr>
<tr>
<td>(0.74, 0.99)</td>
<td>(0.49, 0.77)</td>
<td>(0.50, 0.85)</td>
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<tr>
<td>CANVAS Program[b]</td>
<td>0.86</td>
<td>0.87</td>
<td>0.67</td>
</tr>
<tr>
<td>(0.75, 0.97)</td>
<td>(0.72, 1.06)</td>
<td>(0.52, 0.87)</td>
<td></td>
</tr>
<tr>
<td>DECLARE-TIMI 58[c]</td>
<td>0.93</td>
<td>0.98</td>
<td>0.73</td>
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<tr>
<td>(0.84, 1.03)</td>
<td>(0.82, 1.17)</td>
<td>(0.61, 0.88)</td>
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<tr>
<td>VERTIS-CV[d]</td>
<td>0.97</td>
<td>0.92</td>
<td>0.70</td>
</tr>
<tr>
<td>(0.85, 1.11)</td>
<td>(0.77, 1.11)</td>
<td>(0.54, 0.90)</td>
<td></td>
</tr>
</tbody>
</table>

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GLP-1 Receptor Agonists CVOT

- Liraglutide
- Semaglutide
- Dulaglutide

<table>
<thead>
<tr>
<th>Drug tested</th>
<th>Subjects, n</th>
<th>Duration of follow-up</th>
<th>Baseline HbA1c, %</th>
<th>Cardiovascular risk, %</th>
<th>Main cardiovascular outcomes HR (95%CI)</th>
<th>Primary outcome</th>
<th>NNT</th>
<th>Composite renal outcome measure including macroalbuminuriaHR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELIXA</td>
<td>Lixisentide</td>
<td>6,068</td>
<td>2.1 years</td>
<td>7.7</td>
<td>100</td>
<td>3P-MACE 1.02</td>
<td>0.84</td>
<td>(0.68–1.02)</td>
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<tr>
<td>LEADER</td>
<td>Liraglutide</td>
<td>9,340</td>
<td>3.8 years</td>
<td>8.7</td>
<td>81.3</td>
<td>3P-MACE 0.87</td>
<td>0.78</td>
<td>(0.67–0.92)</td>
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<tr>
<td>SUSTAIN-6</td>
<td>Semaglutide</td>
<td>3,297</td>
<td>2.1 years</td>
<td>8.7</td>
<td>58.8</td>
<td>3P-MACE 0.74</td>
<td>0.64</td>
<td>(0.46–0.88)</td>
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<tr>
<td>EXSCEL</td>
<td>Exenatide  OW</td>
<td>14,752</td>
<td>3.2 years</td>
<td>8.0</td>
<td>73.1</td>
<td>3P-MACE 0.91</td>
<td>0.78</td>
<td>(0.67–0.92)</td>
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<tr>
<td>HARMONY</td>
<td>Albiglutide</td>
<td>9,463</td>
<td>1.6 years</td>
<td>8.7</td>
<td>100</td>
<td>Primary outcome</td>
<td>0.88</td>
<td>(0.76–1.01)</td>
</tr>
<tr>
<td>REWIND</td>
<td>Dulaglutide</td>
<td>9,901</td>
<td>3.1 years</td>
<td>7.3</td>
<td>31.4</td>
<td>Primary outcome</td>
<td>0.85</td>
<td>(0.77–0.93)</td>
</tr>
<tr>
<td>PIONEER-6</td>
<td>Oral Semaglutide</td>
<td>3,183</td>
<td>1.3 years</td>
<td>8.2</td>
<td>84.6</td>
<td>Primary outcome</td>
<td>0.85</td>
<td>(0.77–0.93)</td>
</tr>
</tbody>
</table>

3P-MACE: 3-point major adverse cardiovascular events; NNT: number needed to treat.
### DM DRUG NEW INDICATIONS

#### DRUG CLASS

<table>
<thead>
<tr>
<th>SGLT-2 INHIBITORS:</th>
<th>OTHER INDICATIONS: (IN ADDITION TO T2DM MANAGEMENT)</th>
</tr>
</thead>
</table>
| Invokana (Canagliflozin) | • Risk reduction of major cardiovascular events (eg, cardiovascular death, non-fatal stroke, non-fatal MI) in those with T2DM and established CVD.  
• Risk reduction of end-stage kidney disease, doubling of serum creatinine, or diabetic nephropathy with urinary excretion >300mg/day  
• Risk reduction of hospitalization for heart failure in adult patients with T2DM |
| Invokamet (Canagliflozin/Metformin) | |
| Farxiga (Dapagliflozin) | • Heart failure with reduced ejection fraction → reduces risk of cardiovascular death and hospitalization for heart failure in adults with or without diabetes with heart failure with reduced ejection fraction (NYHA class II to IV) |
| Xigduo (Dapagliflozin/Metformin) | • Risk reduction of hospitalization for heart failure in patients with T2DM and established CVD or multiple cardiovascular risk factors |
| Jardiance (Empagliflozin) | • Risk reduction of cardiovascular mortality (CV death) in adults with T2DM and established CVD |
| GLP-1 AGONISTS: | |
| Ozempic (Saragliptin) | • Risk reduction of major cardiovascular events (3 point MACE)-(eg, CVD, non-fatal MI, non-fatal stroke) in adults with T2DM and established CVD  
• For Trulicity only: includes those with multiple cardiovascular risk factors |
| Victoza (Liraglutide) | |
| Trulicity (Dulaglutide) | |
PEARLS

• Use COMBINATION therapy
  – Target many complementary mechanisms
  – Improve compliance

• Utilize GLP-1 analogs and SGLT-2 inh

• Treating Diabetes is MORE THAN JUST LOWERING blood sugar
  – Prevent COMPLICATIONS- micro AND MACROVASCULAR
2019 update of ADA/EASD consensus report for T2D

"...The decision to treat high-risk individuals with a GLP-1 RA or SGLT2 inhibitor to reduce MACE, HHF, CV death, or CKD progression should be considered independently of baseline HbA1c or individualized HbA1c target."

"...SGLT2 inhibitors are recommended in patients with T2D and heart failure, particularly those with heart failure with reduced ejection fraction, to reduce HHF, MACE, and CVD death, as well as in patients with T2D with CKD to prevent the progression of CKD, HHF, MACE, and CV death."

Hypoglycemia (Non-severe Nocturnal Hypoglycemic Events (NSNHEs))

9 country online survey by adults with diabetes

N=2,108

- 10.4% did not return to sleep that night
- 3.4 hours to return to usual functioning after a NSNHE
- 60.3% needed to take a nap and/or rest the next day
- 21.4% were restricted in their driving the next day
- 39.6% felt “emotionally low” the following day
- 15.8% decreased their insulin dose (over an average of 3.6 days)

Mental, Emotional and Physical Impact

Among 4,540 adults with diabetes (T1D & T2D) who completed the *Hypoglycemic Attitudes and Behavior Scale*...

<table>
<thead>
<tr>
<th></th>
<th>Percentage of adults with diabetes</th>
<th>Estimate of total people affected in the USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not feel confident they can stay safe while driving</td>
<td>33%</td>
<td>9.6 million</td>
</tr>
<tr>
<td>Terrified about passing out in public due to hypoglycemia</td>
<td>13%</td>
<td>3.0 million</td>
</tr>
<tr>
<td>Keep blood glucose higher than recommended to avoid hypoglycemia</td>
<td>17%</td>
<td>3.9 million</td>
</tr>
<tr>
<td>Will eat uncontrollably if they &quot;feel a low&quot;</td>
<td>25%</td>
<td>5.8 million</td>
</tr>
</tbody>
</table>

*The resulting hyperglycemia from these approaches can lead to dangerous, debilitating, and costly complications in the long-term*
Check BS more

- Traditional “fingerstick” glucose testing
- Continuous glucose monitoring (CGM)

**Fingerstick Alone**

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Glucose (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3am</td>
<td>100</td>
</tr>
<tr>
<td>6am</td>
<td>120</td>
</tr>
<tr>
<td>9am</td>
<td>150</td>
</tr>
<tr>
<td>12pm</td>
<td>150</td>
</tr>
<tr>
<td>3pm</td>
<td>120</td>
</tr>
<tr>
<td>6pm</td>
<td>100</td>
</tr>
<tr>
<td>9pm</td>
<td>100</td>
</tr>
</tbody>
</table>

**Continuous Glucose Monitoring**

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Glucose (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3am</td>
<td>100</td>
</tr>
<tr>
<td>5am</td>
<td>120</td>
</tr>
<tr>
<td>9am</td>
<td>150</td>
</tr>
<tr>
<td>12pm</td>
<td>150</td>
</tr>
<tr>
<td>3pm</td>
<td>120</td>
</tr>
<tr>
<td>6pm</td>
<td>100</td>
</tr>
<tr>
<td>9pm</td>
<td>100</td>
</tr>
</tbody>
</table>

Highs missed by these fingersticks
Lows missed by these fingersticks
Meters Accuracy

1035 subjects
3 clinical sites
BG measurements obtained by trained HCPs

18 of the most widely prescribed BG meters and strips were purchased from retail pharmacies

Only 1/3 of the BG meters tested consistently met accuracy standards

ISO 15197-2013 requires 95% of data pairs to be within 15mg/dL <100 mg/dL and 15% for values ≥100 mg/dL
Goal: Replace fingersticks

Sources of Error with SMBG

<table>
<thead>
<tr>
<th>Use Errors</th>
<th>Other Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to wash and dry hands</td>
<td>Marked dehydration</td>
</tr>
<tr>
<td>Sample application errors</td>
<td>Vasoconstriction</td>
</tr>
<tr>
<td>Improper strip storage</td>
<td></td>
</tr>
<tr>
<td>Outdated strips</td>
<td></td>
</tr>
<tr>
<td>Miscoding</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Washed Hands</th>
<th>Exposed Finger (No Washing)</th>
<th>One Alcohol Wipe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peeling an Orange</td>
<td>98 mg/dL</td>
<td>171 mg/dL</td>
<td>118 mg/dL</td>
</tr>
<tr>
<td>Peeling a Grape</td>
<td>93 mg/dL</td>
<td>360 mg/dL</td>
<td>274 mg/dl</td>
</tr>
<tr>
<td>Peeling a Kiwi</td>
<td>90 mg/dl</td>
<td>183 mg/dl</td>
<td>144 mg/dl</td>
</tr>
</tbody>
</table>

#1 – Failure to test
CGM Category

Real-Time CGM (rtCGM)
- Sensor data transmitted continuously to a receiver or display device, which allows for alerts and alarms to be provided to the wearer without any action.

Intermittently Scanned CGM (isCGM)
- Sensor data not transmitted continuously.
- Results are available only when the sensor is scanned with a reading device.
- No automatic alerts.
- Full 24-h data can be captured and downloaded if the sensor is scanned at least every 8 hours.
CGM lowers BS regardless of Insulin Delivery Method

Know Your Arrows

Based on the previous 30 minutes:

- Glucose is changing less than 1mg/dL each minute
- Glucose could increase 30-60mg/dL
- Glucose could decrease 30-60mg/dL
- Glucose could increase more than 90 mg/dL
- Glucose could decrease more than 90 mg/dL
Arrows Help Forecast Glucose Levels

- 50-80 mg/dL
- ≥235 mg/dL
- 91-121 mg/dL
Prediction Alerts = 15 minutes warning
Threshold alert = 5 minutes warning
## 2020 Medicare CGM Coding

<table>
<thead>
<tr>
<th>Codes / Description</th>
<th>Medicare&lt;sup&gt;1&lt;/sup&gt; Physician Office Fee Schedule</th>
<th>Medicare&lt;sup&gt;2&lt;/sup&gt; Outpatient Diabetes Center</th>
<th>Private Payer&lt;sup&gt;3&lt;/sup&gt; (2019 Averages)</th>
<th>Relative Value Unit (RVU) Non-Facility&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CPT 95249 (Personal CGM - Startup/Training)</strong></td>
<td>$55.58</td>
<td>$55.01 APC 5733</td>
<td>$127</td>
<td>1.54</td>
</tr>
<tr>
<td>Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; patient-provided equipment, sensor placement, hook-up, calibration of monitor, patient training, and printout of recording. <em>Bill only once during the time period that the patient owns the device.</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CPT 95250 (Professional CGM)</strong></td>
<td>$152.86</td>
<td>$115.93 APC 5012</td>
<td>$304</td>
<td>4.23</td>
</tr>
<tr>
<td>Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; physician or other qualified health care professional (office) provided equipment, sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording. <em>Do not bill more than 1x/month.</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CPT 95251 (CGM Interpretation)</strong></td>
<td>$36.81</td>
<td>Paid under physician fee schedule</td>
<td>$96</td>
<td>1.02</td>
</tr>
<tr>
<td>Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; analysis, interpretation and report. <em>Do not bill more than 1x/month.</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Evaluation and Management (E/M)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CPT 99212-99215</strong></td>
<td>$45.19-$148.33</td>
<td>$82-$279</td>
<td>1.28-4.11</td>
<td></td>
</tr>
<tr>
<td>For an established patient in non-facility or office setting. Appropriate code to be determined by the office.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Individualized Therapies

<table>
<thead>
<tr>
<th>Hypoglycemia</th>
<th>Cost</th>
<th>Weight Gain</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Metformin</td>
<td>Metformin</td>
<td>Metformin</td>
</tr>
<tr>
<td>DPP-IV inhibitors</td>
<td>Sulfonylurea</td>
<td>DPP-IV inhibitors</td>
<td>Insulin</td>
</tr>
<tr>
<td>GLP-1</td>
<td>NPH insulin</td>
<td>GLP-1 Analogs</td>
<td>Sulfonylurea</td>
</tr>
<tr>
<td>TZD</td>
<td>Regular Insulin</td>
<td></td>
<td>Actos</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>GLP-1</td>
</tr>
</tbody>
</table>
Clinical Pearls Summary

1. Tumor size correlates with prolactin level
2. Strong inverse correlation between pth and calcium
3. Always ask for wrist DXA when suspecting primary hyperparathyroidism
4. Always check TSH when thyroid nodule(s) are present
Clinical Pearls Summary Cont.

5. **NO** thyroid uptake and scan (RAIU) unless TSH is **LOW**

6. **Methimazole** is the anti-thyroid Drug of Choice (DOC)

7. Check thyroid peroxidase antibodies (tpo abs) in hypothyroid patients

8. All pregnant women with tpo abs **POSITIVE** need to be treated to bring TSH < 2
Clinical Pearls Summary Cont.

9. Use and stick to one brand of thyroid medication

10. Suggested regimen: Metformin +/- SGLT-2 an/or GLP-1 analogs

11. Utilize more CGMs- It’s more important than insulin pumps.
Thank God he stopped talking!
Contact

• QTN303@GMAIL.COM
• 602-697-2044 (cell)