

The Cortisol Reports

Episode 2 - Applying Advances in Practice:
Case-Based Look at Selecting Therapy for Cushing Syndrome

Case 1

Cushing Syndrome

Case 1: 72-Year-Old Male Retired Firefighter

- BMI 43
- PMHx – CAD s/p MI with PCI 2023, DM2, HTN, former smoker, obesity
- Meds –
 - aspirin 81 mg cap
 - carvedilol (COREG) 25 MG tablet
 - clopidogrel (PLAVIX) 75 mg tablet
 - dapagliflozin propanediol (FARXIGA) 10 mg tablet
 - dulaglutide (TRULICITY) 1.5 mg/0.5 mL syringe
 - fenofibrate (TRICOR) 145 MG tablet
 - Fiasp FlexTouch U-100 Insulin 100 unit/mL (3 mL) inpn
 - fluticasone propionate (FLONASE) 50 mcg/actuation nasal spray
 - folic acid (FOLVITE) 1 MG tablet
 - glimepiride (AMARYL) 4 MG tablet
 - insulin glargine (LANTUS, SEMGLEE) 100 unit/mL injection
 - losartan (COZAAR) 100 MG tablet
 - magnesium oxide (MAG-OX) 400 mg tablet
 - metoprolol tartrate (LOPRESSOR) 50 MG tablet
 - niacin (SLO-NIACIN) 500 mg tablet
 - omega-3 fatty acids (LOVAZA) 1 gram capsule
 - pantoprazole (PROTONIX) 20 MG tablet
 - pentoxifylline (TRENTaL) 400 mg CR tablet
 - pioglitazone (ACTOS) 15 MG tablet
 - rosuvastatin (CRESTOR) 40 MG tablet
 - tadalafil (TADALAFIL ORAL) 5 MG tablet
 - tirzepatide (MOUNJARO) 2.5 mg/0.5 mL pnij

Postoperative Assessment and Management

- Postoperatively, most patients require glucocorticoid replacement
- Cortisol levels are monitored after surgery
- Glucocorticoid replacement is initiated when cortisol drops below 10 and blood pressure softens
- At least 90% of profound cases need postoperative steroid replacement
- Determining glucocorticoid need in mild hypercortisolism is more challenging
- Patients are kept overnight for observation
 - ACTH stimulation testing is performed

72-Year-Old Male Retired Firefighter

- CT scan obtained for flank pain (kidney stone)
 - Incidental 2.1cm R adrenal lesion
- LDST – 8am cortisol 5.7, Dex 373
- Plasma Normetanephrines 301 (0 – 218), metanephrines 123 (0 – 88), Aldo 7 (0 – 30), Renin 1.1 (0.167 – 5.4)
- ACTH 11, DHEA 27
- HgbA1C – 8.2 (up from 7.8)
- Cr 1, BUN 16

Recent Data on Surgery Treatment Success

	All CS, n = 296	ACS, n = 84	ECS, n = 27	CD, n = 185
First-line surgical therapy, n (%)	284 (96)	83 (99) ADX, unilateral adenoma: 53/54 BADX, MiBAH: 7/7 BADX, PBMAH: 4/23 ADX, PBMAH: 18/23 BADX, PBMAH: 1/23	21 (78) Tumor resection: 16 (59) BADX: 3 (11) unnecessary TSS: 2 (7)	180 (97) TSS: 175 (95) BADX: 5 (3)
First-line medical therapy	11 (4)	Osilodrostat: 1	Metyrapone: 6 (22) Additional ketoconazole: 4 (15)	Pasireotide: 2 seconds.c.(1) Cabergoline: 3 (2)
Persistence	54 (18)	5 (6)	4 (15)	45 (24)
Recurrence	40 (14)	3 (4)	4 (15)	33 (18)
Second-line therapy		ADX li: 1 Metyrapone: 2 Osilodrostat: 1 No therapy: 4 (mild CS, patients' preference)	Tumor resection: 2 BADX: 4 Metyrapone: 1 Other medications: 1	TSS: 31 BADX: 10 Radiation: 8 Pasireotide: 14 (8 seconds.c., 6 LAR) Cabergoline: 3 Metyrapone: 6 Osilodrostat: 4 Ketoconazole: 8 Other medications: 5
No remission	52	6	2	44
Further lines of therapy		Metyrapone: 2 Osilodrostat: 1 No therapy: 3 (mild CS, patients' preference)	Tumor resection: 1 BADX: 2	TSS: 10 BADX: 18 Radiation: 8 Pasireotide: 5 (2 seconds.c., 2 LAR, 1 both) Cabergoline: 4 Metyrapone: 10 Osilodrostat: 4 Ketoconazole: 6
No remission	20	5	0	15

Abbreviations: ACS, adrenal Cushing's syndrome; ADX, adrenalectomy; BADX, bilateral adrenalectomy; CD, Cushing's disease; CS, Cushing's syndrome; ECS, ectopic Cushing's syndrome; LAR, long-acting release; MiBAH, micronodular bilateral adrenal hyperplasia; PBMAH, primary bilateral macronodular adrenal hyperplasia; TSS, transphenoidal surgery.

Medical Therapies for Cushing's Syndrome

Start with anticortisol agents at a low dose to start prepping that patient and moving that patient towards surgery

Glucocorticoid Receptor Blocker/Modulator

- ✓ Mifepristone
- ⚠ Relacorilant
(CRL Dec 2025- more to come)



Adrenal-Directed Agents: Steroidogenesis Inhibitors

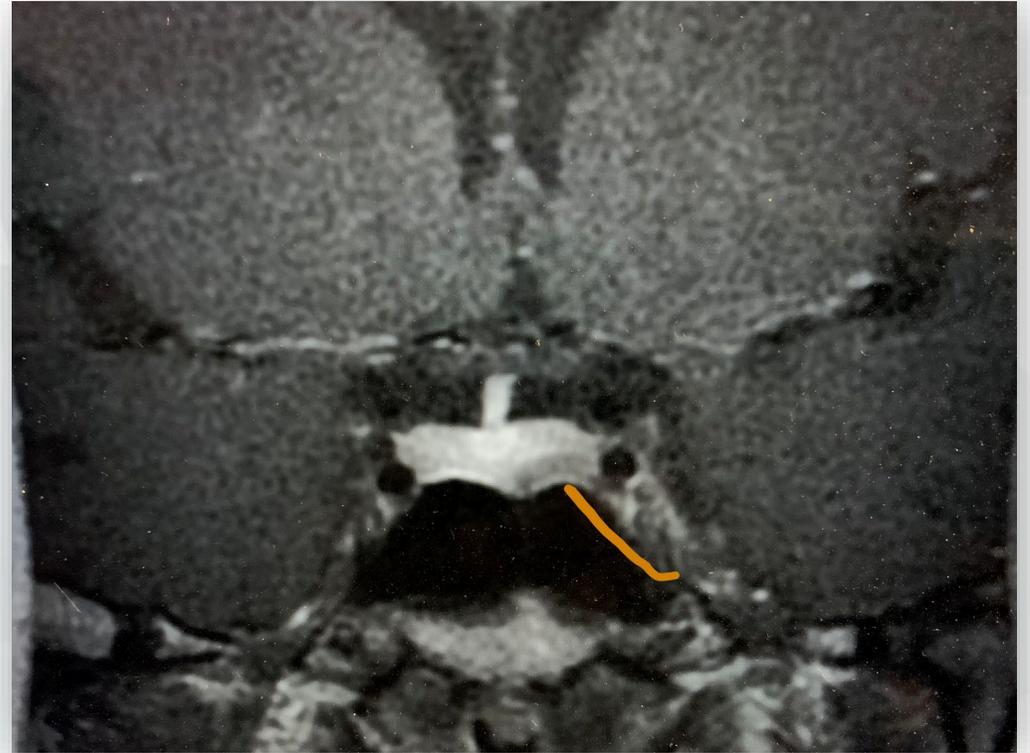
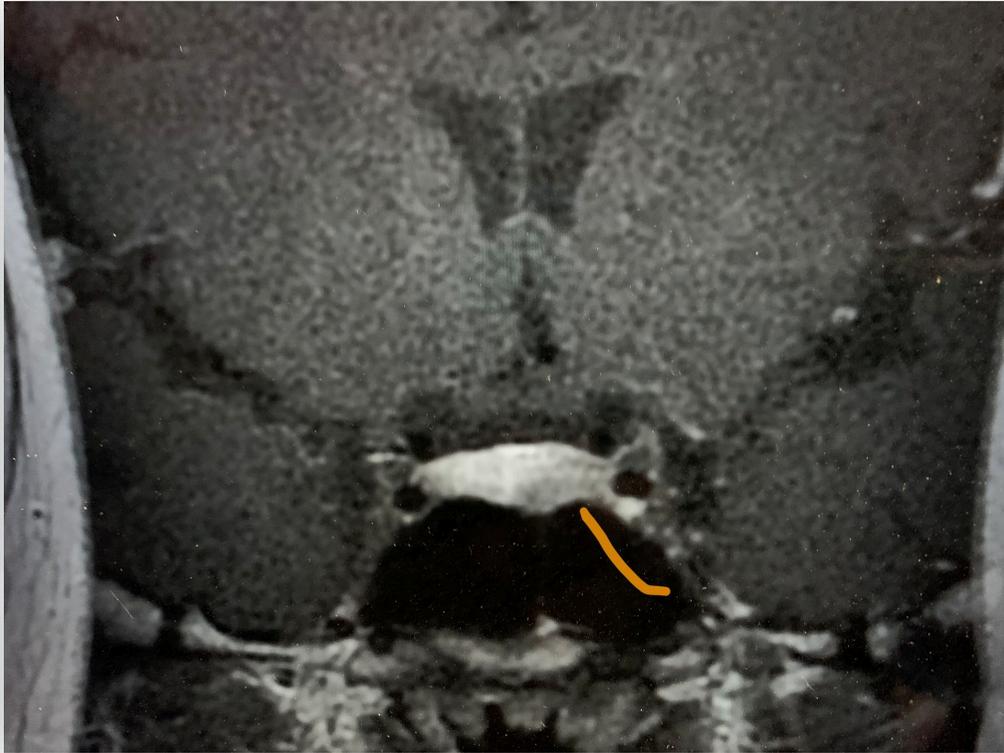
- ✓ Osilodrostat
- ✓ Levoketoconazole
- ⚠ Ketoconazole
- ⚠ Metyrapone
- ⚠ Mitotane
- ⚠ Etomidate

- ✓ Licensed in US for Cushing's indications
- ⚠ Used off-label

Case 2

Cushing Disease

Case 2: A 36-Year-Old Woman with CD



36-Year-Old Woman

- Gross total resection of an ACTH-immunopositive tumor
- Postoperative serum cortisol 1 mcg/dL
- Required steroid supplementation for 2 years until recovery of HPA function proved by low-dose ACTH stimulated cortisol 21 mcg/dL
- Lost 45 pounds in one year
- Initial recovery 24h UFC 18 mcg
- Lost to follow-up for 2 years

My Approach to the Postoperative Evaluation

- 8AM serum cortisol levels
- When 8 AM cortisol over 7mcg/dL then 1 mcg low dose ACTH stimulation test

When patient off steroids and undergoing long-term follow-up:

- Urine Free Cortisol
- 1mg Dexamethasone Suppression Test (DST)
- Salivary cortisol profile or late night salivary cortisol (LNSC)

36-Year-Old Woman

- Presented for follow-up with complaints of insomnia, weight gain
- No cushingoid features on examination
- 24h UFC 41 mcg

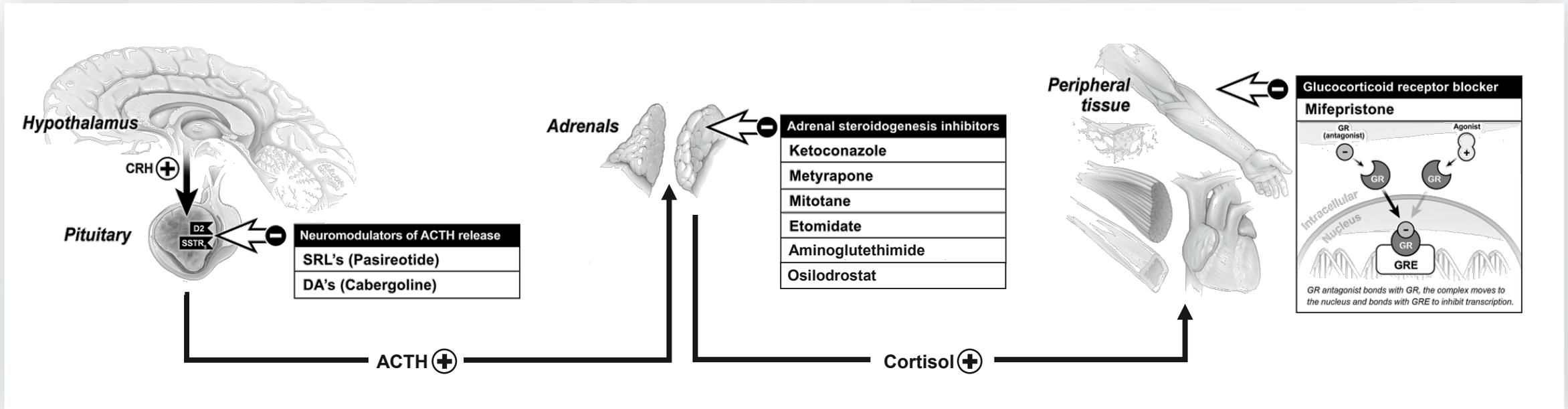
36-Year-Old Woman



Cushing's Disease: Surgical Results

First Author	n	Cure (%)	Recurrence (%)	Mean f/u (m)
Invitti	288	69	17	
Bochicchio	668	76	13	46
Blevins	96	85	16	49
Sonino	103	77	26	72
Mampalam	216	79	5	46
Swearingen	161	85	7	24
Nakane	100	92	9	39
Hammer	289	82	9	131

Medical Therapy



Medical Therapies for Cushing's Syndrome

Pituitary-Directed Agents

✓ Pasireotide (subQ and LAR)

⚠ Cabergoline



Glucocorticoid Receptor Blocker/Modulator

✓ Mifepristone

⚠ Relacorilant
(CRL Dec 2025- more to come)



Adrenal-Directed Agents: Steroidogenesis Inhibitors

✓ Osilodrostat

✓ Levoketoconazole

⚠ Ketoconazole

⚠ Metyrapone

⚠ Mitotane

⚠ Etomidate



- ✓ Licensed in US for Cushing's indications
- ⚠ Used off-label

Cushing Disease/Syndrome: Perioperative Management

