# 30 YEAR OLD FEMALE WITH HYPOKALEMIA

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Endorama

8/30/2012

# HPI

- 30 yo AA female G6P4 currently 24 weeks pregnant with a hx of HTN, type 2 diabetes, admitted to OB service with back pain, hypokalemia, consulted to help evaluate cause of hypokalemia
- OB service questioning if her diabetes could be contributing to hypokalemia.
- Her K has been persistently low since June 2012, as low at 2.4 on admission. No data on K prior to pregnancy.
- She has required aggressive K supplementation since admission.
- Received 120 MeQ after which K increased to 3.
- Denies nausea, vomiting, diarrhea, headache, visual problems.

# HPI continued...

- She denies any history of adrenal problems in the past. She has never had an aldosterone or renin level checked in the past and no imaging performed of adrenal glands.
- She is currently on labetalol 300 mg po q8h for management of her hypertension. She was diagnosed with HTN at age 19.
- Prior to pregnancy, she reports she was taking 3 different blood pressure medications, but cannot recall the names.
- She states her bp meds have been changed multiple times in the past with her prior pregnancies.

# HPI continued…

- Her diabetes was diagnosed 8 months ago by routine testing by her PCP.
- She was initially started on metformin and then started on insulin when she became pregnant.
- She is currently on NPH 54 units QAM and 22 units QPM as well as regular insulin 28 units QAM and 22 units QPM.
- Her most recent A1c on 1 month ago was 6.8%. Her fingersticks have been reasonably well-controlled during this admission and she reports good control at home as well.

# HPI continued...

- She also reports persistent back pain "all over her back" for past 3 weeks, which has continued during this admission.
- Associated numbness on face and lower extremities and some lower extremity weakness requiring the use of a cane at times
- No slurred speech, no vision problems. Denies mood changes or recent stressors in life.

# PMHx

**Past Medical History**

- • Type 2 Diabetes (dx 8 mo. ago in 2011 by routine blood tests with some neuropathy, no retinopathy or nephropathy)
- • Hypertension (dx *in 2002)*

**Past Surgical History**

- Cholecystectomy; 2009
- Appendectomy; 1998
- Cesarean delivery 2002, 2004, 2007

# Family Hx, Social Hx, Allergies

## Family Hx

-Mother- type 2 diabetes, dx with HTN at early age in 20s
-MGM- type 2 diabetes, also dx with HTN at early age in 20s
-Sister-type 2 diabetes, HTN, dx in 20s
-Father-healthy

## Social Hx

•Single and lives with her 4 children, ages 10, 8, and 5 year old twin boys

•Used to work at Target, currently not employed

•Smoking status:• Never Smoker

•Alcohol Use: Denies

•Drug Use: Denies

**ALLERGIES :** Penicillin-> hives, pruritis and rash

# Medications

*Current Scheduled Medications*

- docusate 100 mg Oral TID (09,13,17)
- insulin human NPH 22 Units Subcutaneous QPM (17)
- insulin human NPH 54 Units Subcutaneous QAM (08)
- insulin human regular 22 Units Subcutaneous QPM (17)
- insulin human regular 28 Units Subcutaneous QAM (08)
- labetalol 300 mg Oral TID (09,13,17)
- potassium chloride 60 mEq Oral ONCE

Home Meds:

Labetalol 300 mg po TID

NPH/Regular insulin 54u/28u QAM and 22u/22u qpm

# Physical Exam

- VS: Temp 98.4 $^{0}$F, BP 132/63, HR 82, RR 20, O2 sat 96% on RA, weight 111.5 kg  Height 165 cm  BMI 40.9
- Gen:NAD, obese
- HEENT: NCAT, Eomi
- Neck: supple, no thyromegaly
- Heart: +S1/S2, no murmurs
- Lungs: Cta b/l
- Abdomen: soft, gravid, no fundal tenderness
- Extremities: no c/c/e,normal muscle tone and strength
- Neuro: alert and oriented x 3, cranial nerves intact, reflexes normal
- Back: Tender to light touch all over back; per Neuro note-no pain when distracted ; rectal tone normal
- Skin: flesh colored striae on abdomen (no hyperpigmentation)
  No acne or hirsutism noted

# Labs

137| 102 | 23 / 117 Ca 9.0 (8.5- 10.2 mg/dl)

2.4 | 23 |0.4 \ Mg 1.7 (1.6-2.5 mg/dl)

Phos 2.7 (2.4- 4.4 mg/dl)

Albumin 3.8 (3.5-5 g/dl)

A1c- 6.8%

TSH- 1.16 (0.3- 4 mcU/ml)

8.8 \ 10.5 /225

/ 30.6 \

**Major causes of hypokalemia**

| |
|---|
| **Decreased potassium intake** |
| **Increased entry into cells** |
| An elevation in extracellular pH |
| Increased availability of insulin |
| Elevated β-adrenergic activity - stress or administration of beta agonists |
| Hypokalemic periodic paralysis |
| Marked increase in blood cell production |
| Hypothermia |
| Chloroquine intoxication |
| **Increased gastrointestinal losses** |
| Vomiting |
| Diarrhea |
| Tube drainage |
| Laxative abuse |
| **Increased urinary losses** |
| Diuretics |
| Primary mineralocorticoid excess |
| Loss of gastric secretions |
| Nonreabsorbable anions |
| Renal tubular acidosis |
| Hypomagnesemia |
| Amphotericin B |
| Salt-wasting nephropathies - including Bartter's or Gitelman's syndrome |
| Polyuria |
| **Increased sweat losses** |
| **Dialysis** |
| **Plasmapheresis** |

UpToDate

## Characteristics of the different types of renal tubular tubular acidosis

| | Type 1 RTA | Type 2 RTA | Type 4 RTA |
|---|---|---|---|
| Primary defect | Impaired distal acidification | Reduced proximal bicarbonate reabsorption | Decreased aldosterone secretion or effect |
| Plasma bicarbonate | Variable, may be below 10 meq/L | Usually 12 to 20 meq/L | Greater than 17 meq/L |
| Urine pH | Greater than 5.3 | Variable, greater than 5.3 if above bicarbonate reabsorptive threshold | Usually less than 5.3 |
| Plasma potassium | Usually reduced but hyperkalemic forms exist; hypokalemia largely corrects with alkali therapy | Reduced, made worse by bicarbonaturia induced by alkali therapy | Increased |

UpToDate

# Type 4 RTA (hyporeninemic hypoaldosteronism)

- By far the most common cause of hypoaldosteronism
- Commonly seen in patients with diabetes with mild renal impairment
- Hyperkalemia and metabolic acidosis are out of proportion to the degree of renal impairment.
- Caused by deficiency in renin production
- K would >5 and usually seen after 15-20 years of diabetes associated with fibrosis of zona glomerulosa
- Aldosterone and renin levels fail to increase normally after salt restriction and volume contraction.
- Pathogenesis is uncertain; possibilities include:
  - Renal disease
  - Autonomic neuropathy
  - Extracellular fluid volume expansion
  - Defective conversion of renin precursors to active renin

# Recommendations

- Recommend checking renin and aldosterone level
- Unlikely to be caused by diabetes since would expect type 4 RTA resulting in hyperkalemia due to hypoaldosteronism
- Consider hyperaldosteronism given multiple family members with HTN at early age.
- Low sodium diet, less than 2400 mg/day
- Minimum of 3-4 high potassium containing foods/day

# Adrenal Disease in Pregnancy

- Relatively rare, yet can lead to significant maternal and fetal morbidity
- Making diagnosis challenging because fetal-placental unit  alters the maternal endocrine metabolism and hormonal feedback mechanisms

# Pregnancy and the HPA axis

- Both maternal and placental ACTH and cortisol levels rise dramatically during pregnancy, with initial surge at 11$^{th}$ week of gestation, significant rise after 16-20 weeks, and final surge of these hormones during labor.
- The fetoplacental unit has a marked capacity for steroidogenesis, causing plasma cortisol levels to rise 2-3 fold over the course of the pregnancy above the levels of non-pregnant controls, reaching values in the range seen in Cushing's syndrome
- Increased estrogens from placenta stimulate CBG levels, leading to increase in total cortisol and decrease in cortisol clearance. As cortisol is displaced from CBG by progesterone, free cortisol levels also increase.

# Pregnancy and the Renin-Angiotensin System (RAS)

- Plasma renin activity increases early in the 1st trimester, reaching values 3-7 fold above the normal range by the 3rd trimester.
- Plasma aldosterone levels increase 5-20 fold during gestation, with a plateau at 38 weeks.
- As GFR and progesterone increase, aldosterone also increases promoting sodium retention at the distal renal tubules
- Deoxycorticosterone (DOC), a potent mineralocorticoid, increases 2-fold normal in early pregnancy to 60-100ng/100 ml in 3rd trimester, which may contribute to sodium retention in pregnancy.

# Hospital Course

- K remained stable in 3's with daily replacement for 2 days
- Evaluated by Neurology → no neurologic cause of back pain
- "Her exam is difficult to localize to a single neurological lesion, and is concerning for factitious vs conversion disorder or somatization disorder. Recommend Psych evaluation."

# Hospital Course

- Psych Eval—
  -revealed pregnancy was unexpected
  - patient thought the father of the child "trapped her" by tampering with the condom used for protection.
  -did not want another child because she is not financially stable.
  -Had thoughts about terminating the pregnancy but ultimately decided against it because of potential complications to herself with her comorbidities.
  -will be having a sterilizing procedure after delivery in order to prevent conception of any more children.

- Diagnosis of Somatoform Disorder, Not Otherwise Specified.

- Patient persistently declined counseling and pysch f/u.

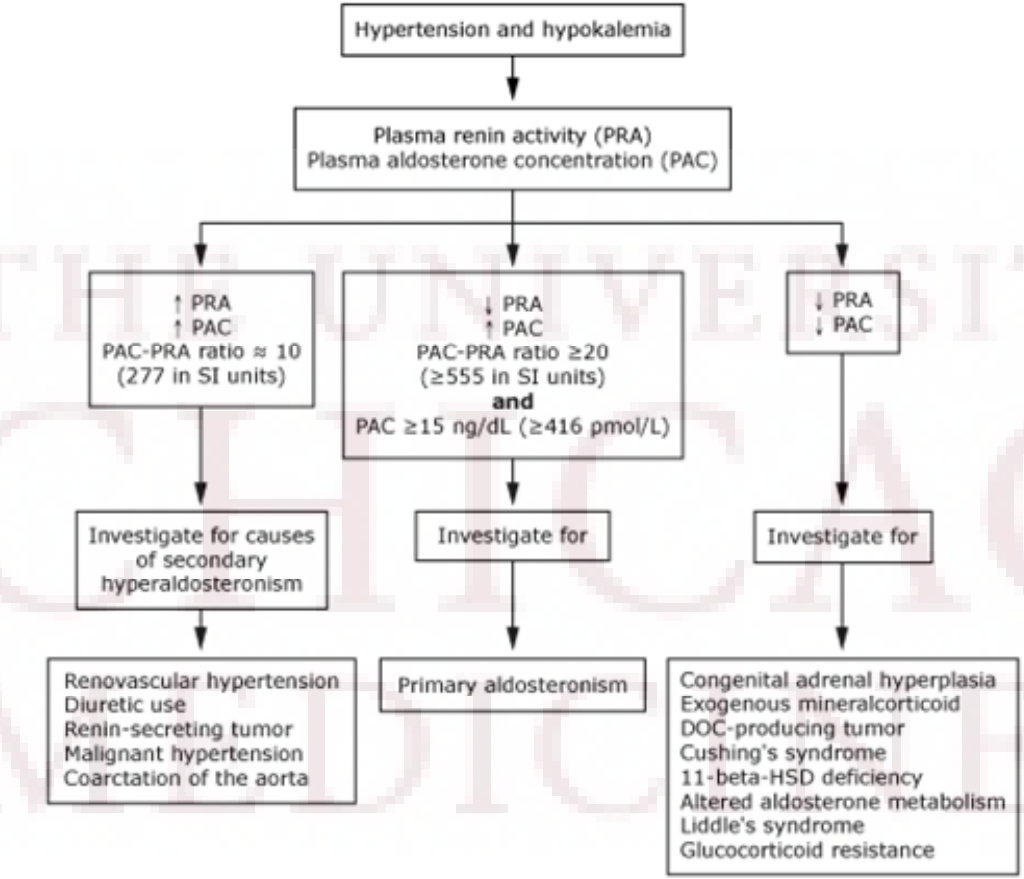
# Hospital Course

- Patient discharged home with outpatient f/u.
- Has weekly f/u in high risk OB.
- Has upcoming Endo appointment for further eval.

# Additional Lab Results

- Renin- 1.9 (Na-replete Mean: 1.9, range 0.6-4.3 ng/ml/h)
- Aldosterone <4 (<21 ng/dl)
- K: 3.0
- Mg: 1.7

## PAC/PRA ratio in hypertension and hypokalemia

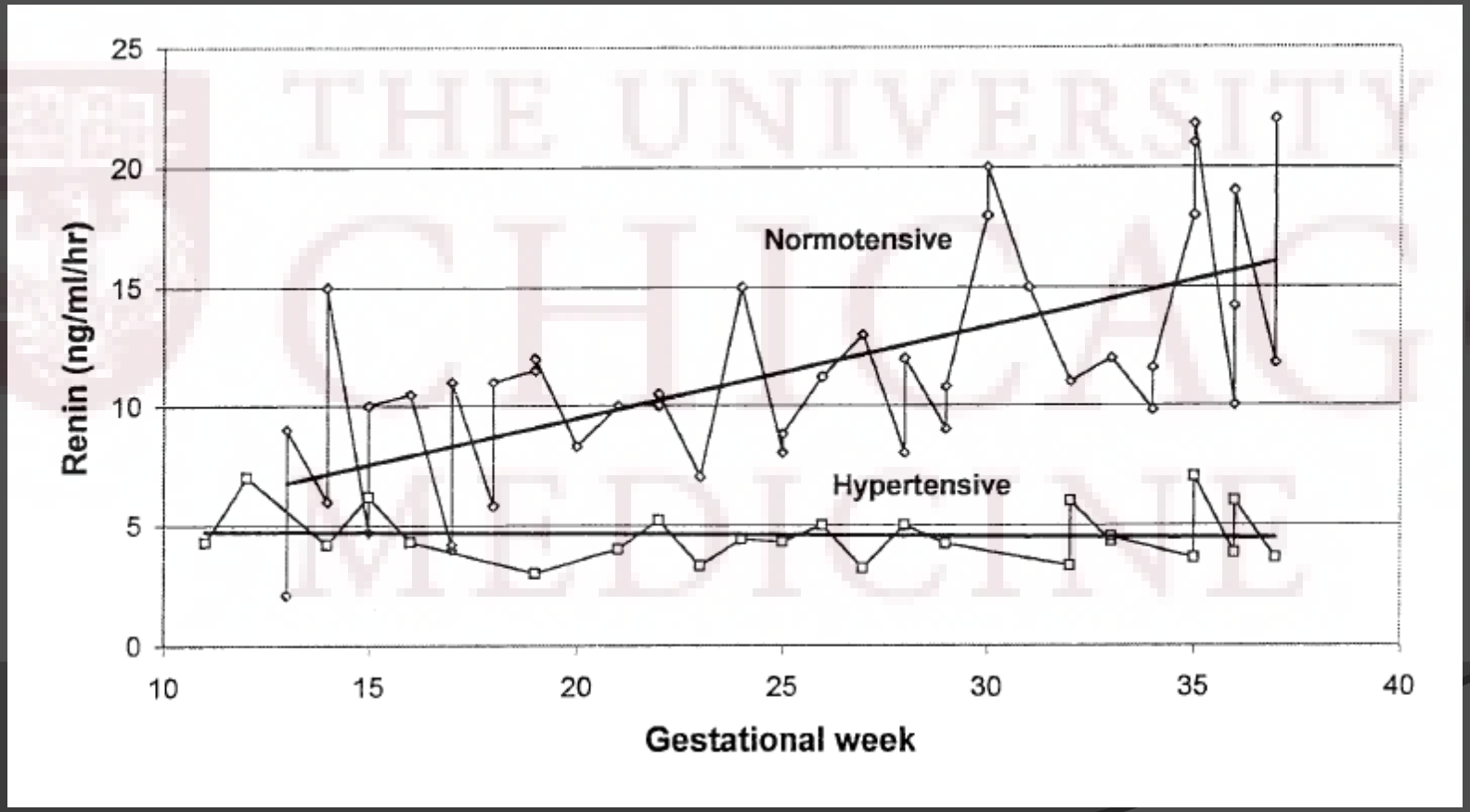



Use of the plasma aldosterone concentration (PAC)-to-plasma renin activity (PRA) ratio to differentiate among different causes of hypertension and hypokalemia.

*Adapted from: Young, WF Jr, Hogan, MJ, Renin-independent hypermineralocorticoidism. Trends Endocrinol Metab 1994; 5:97.*

UpToDate

# Plasma Renin Activity in Normotensive and Hypertensive Pregnant Women




Elsheik A, Creatsas G, Mastorakos G, Milingos S, Loutradis D, Michalas S. *The renin-aldosterone system during normal and hypertensive pregnancy.* Arch Gynecol Obstet 2001 Jan;264(4):182-5.

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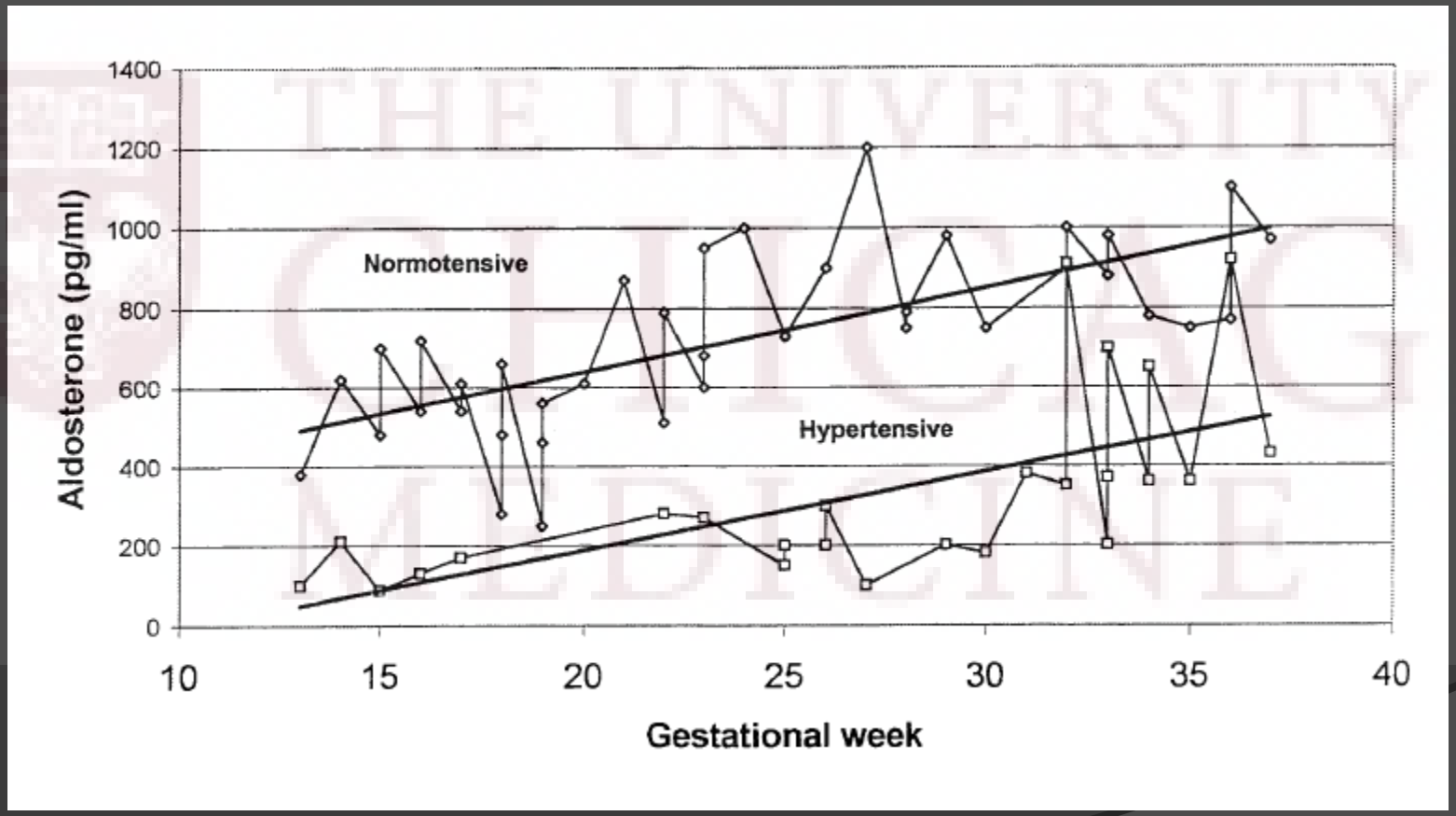


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# Take Home Points

- Type IV RTA, associated with diabetes, usually results in hyperkalemia, not hypokalemia due to hyporeninemic hypoaldosteronism.
- Adrenal disorders are difficult to diagnose in pregnancy because the fetal-placental unit alters the maternal endocrine metabolism and hormonal feedback mechanisms
- In normotensive pregnant patients, plasma renin activity increases early in the 1st trimester, reaching values 3-7 fold above the normal range by the 3rd trimester. Plasma aldosterone levels increase 5-20 fold during gestation, with a plateau at 38 weeks.
- The characterization of the renin-aldosterone system in hypertensive pregnancy is less clear.

# References


- 1. Daesman Suri, Jill Moran, Judith U. Hibbard, Kristen Kasza, and Roy E. Weiss. *Assessment of Adrenal Reserve in Pregnancy: Defining the Normal Response to the Adrenocorticotropin Stimulation Test. The Journal of Clinical Endocrinology & Metabolism October 1, 2006 vol. 91 no. 10 3866-3872.*
- ***2.*** Lekarev O and New MI. *Adrenal disease in pregnancy.* Best Pract Res Clin Endocrinol Metab. 2011 Dec;25(6):959-73.
- 3. Young, WF Jr, Hogan, MJ, Renin-independent hypermineralocorticoidism. Trends Endocrinol Metab 1994; 5:97.
- 4. Elsheik A, Creatsas G, Mastorakos G, Milingos S, Loutradis D, Michalas S. *The renin-aldosterone system during normal and hypertensive pregnancy.* Arch Gynecol Obstet 2001 Jan;264(4):182-5.

# Cushing's Syndrome in Pregnancy

- Rare in pregnancy because hypercortisolism inhibits normal ovulation. In pituitary disease, there is altered gonadotropin secretion and in adrenal disease, there is secretion of adrenal androgens.
- ~140 cases of Cushing's syndrome has been reported overall with 18 weeks being mean gestation age.
- Adrenal adenomas comprise of 40-50% of cases
- In many cases, Cushing's syndrome first becomes evident during pregnancy with improvement or resolution of symptoms during delivery
- Theory is that placental rise in CRH is instrumental in manifestation and exacerbation of symptoms.

# Cushing's syndrome in Pregnancy

- Diagnosis challenging because typical symptoms may overlap including central weight gain, edema, fatigue, emotional upset, hypertension, and glucose intolerance.
- Hyperpigmented violaceous striae as opposed to skin-colored striae can help differentiate between Cushing's syndrome and pregnancy
- Diagnosis complicated by physiologically elevated levels of total serum cortisol, serum and urine free cortisol, and ACTH