# INTEGRATING CONVENTIONAL AND FUNCTIONAL MEDICINE IN COMPLEX ENDOCRINE CONDITIONS

The Art of Integration

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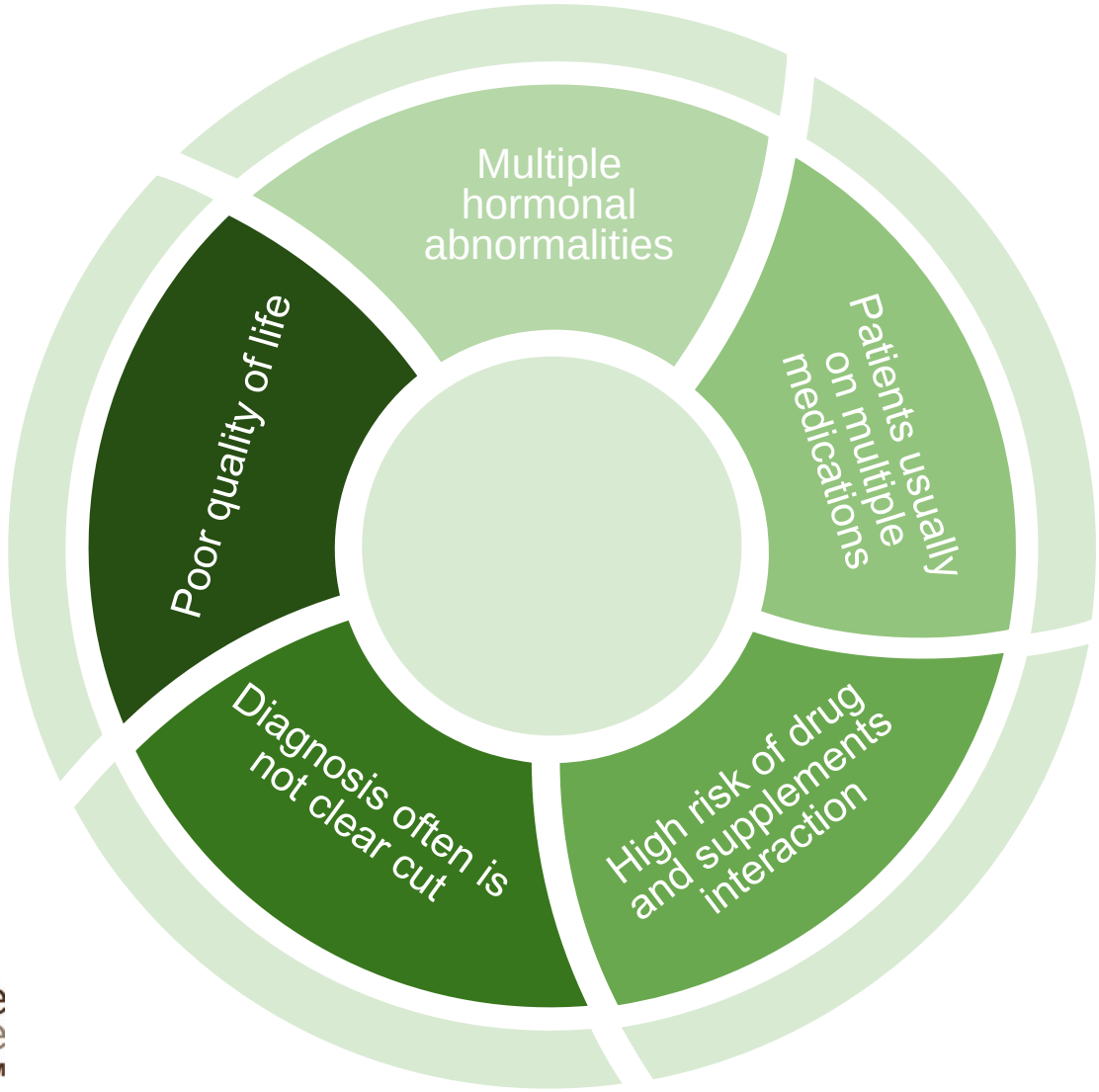
# Characteristics Of Chronic Complex Endocrine Patients

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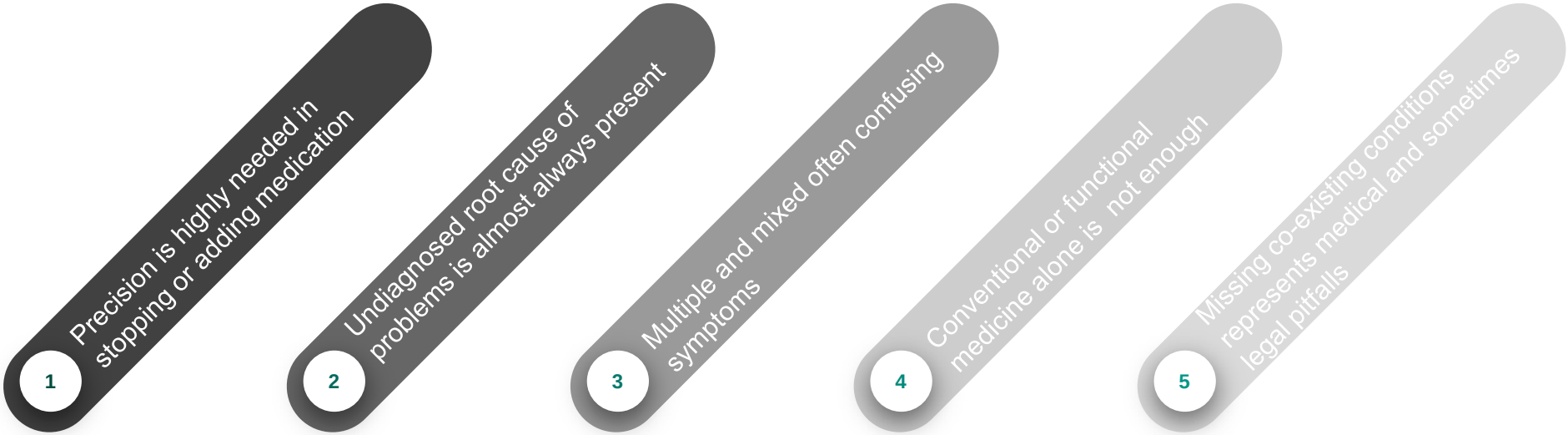
# Challenges Of These Types Of Patients

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# Overlapping And Sometimes Overlooked Endocrine Issues

- Uncommon types of insulin resistance
    - Type A insulin resistance (and C)
    - Type B insulin resistance

- Polycystic ovarian syndrome (PCOS) and high androgen states
- High prolactin levels and pituitary tumors

# How Do We Overlook This In Functional Medicine

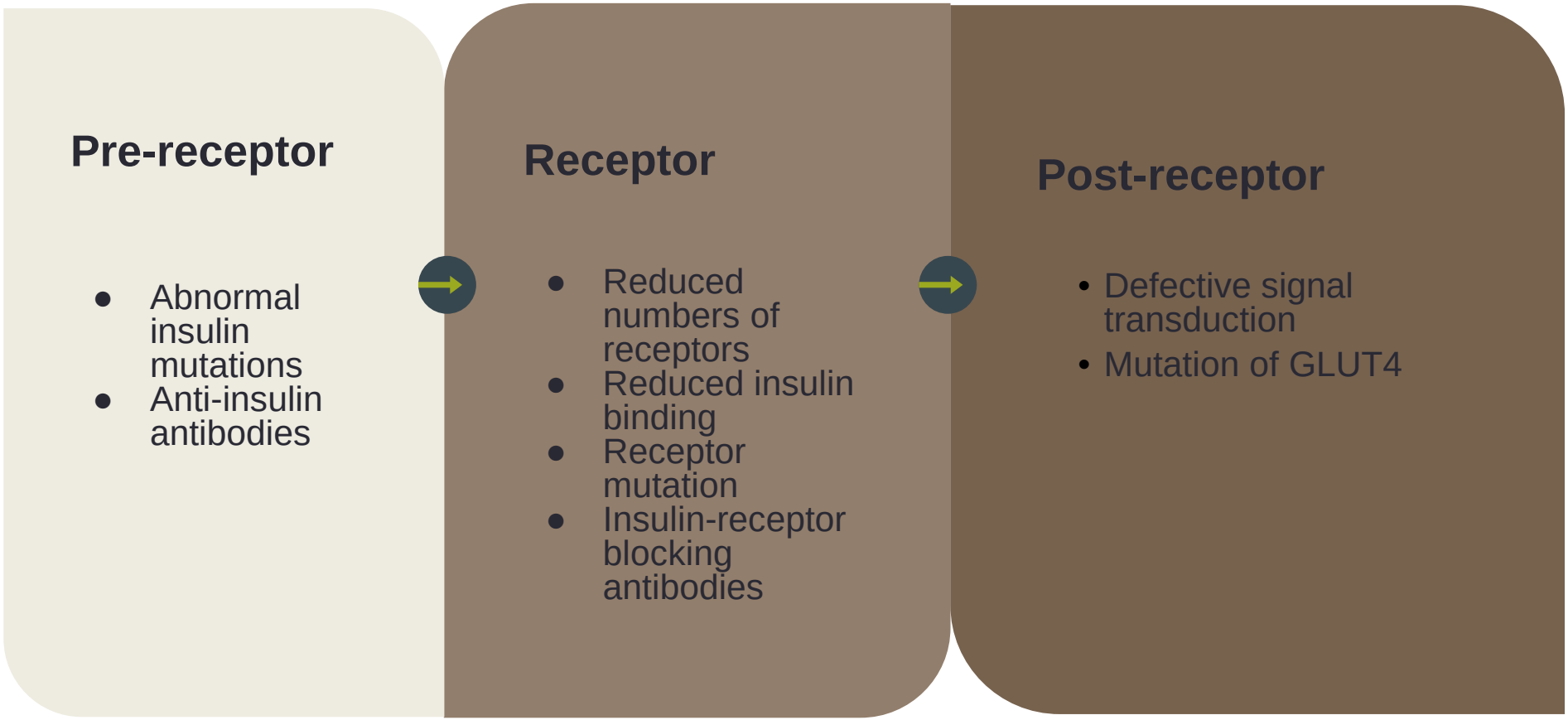
- Lack of awareness of these conditions
- Great focus on food allergies and intolerances
- Great focus on nutrients deficiencies and supplements
- Lack of full understanding of the hormonal interplay (Mds and non Mds)

# Insulin Resistance (IR)

**Definition:** Insulin resistance is defined as “a state in which a greater than normal amount of insulin is required to elicit a quantitatively normal response”

- IR occurs in association with several physiological and pathological states like Obesity, NIDDM, PCOS, metabolic syndrome and the uncommon syndromes of extreme IR.
- Complicating things further, insulin resistance can be selective, *i.e.* involving only certain aspects of insulin action (pre-receptor, receptor and postreceptor resistance).

# IR Classification According To Receptor Site

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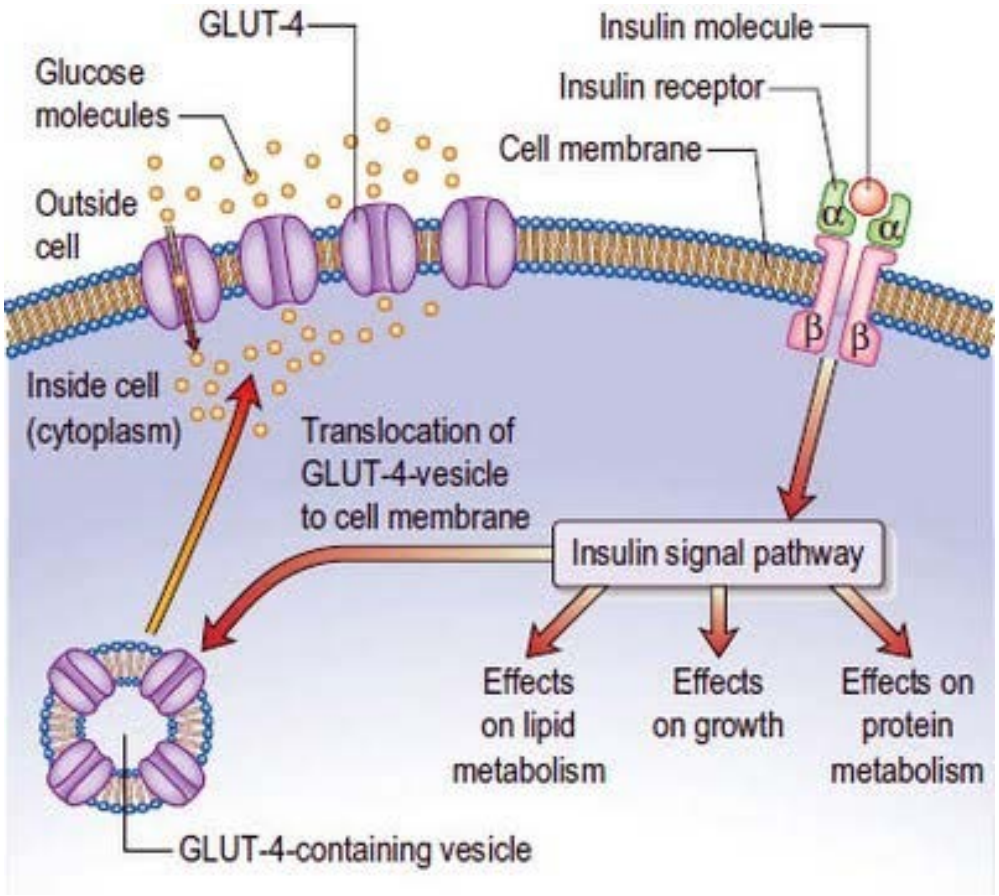
# Insulin Resistance (IR)

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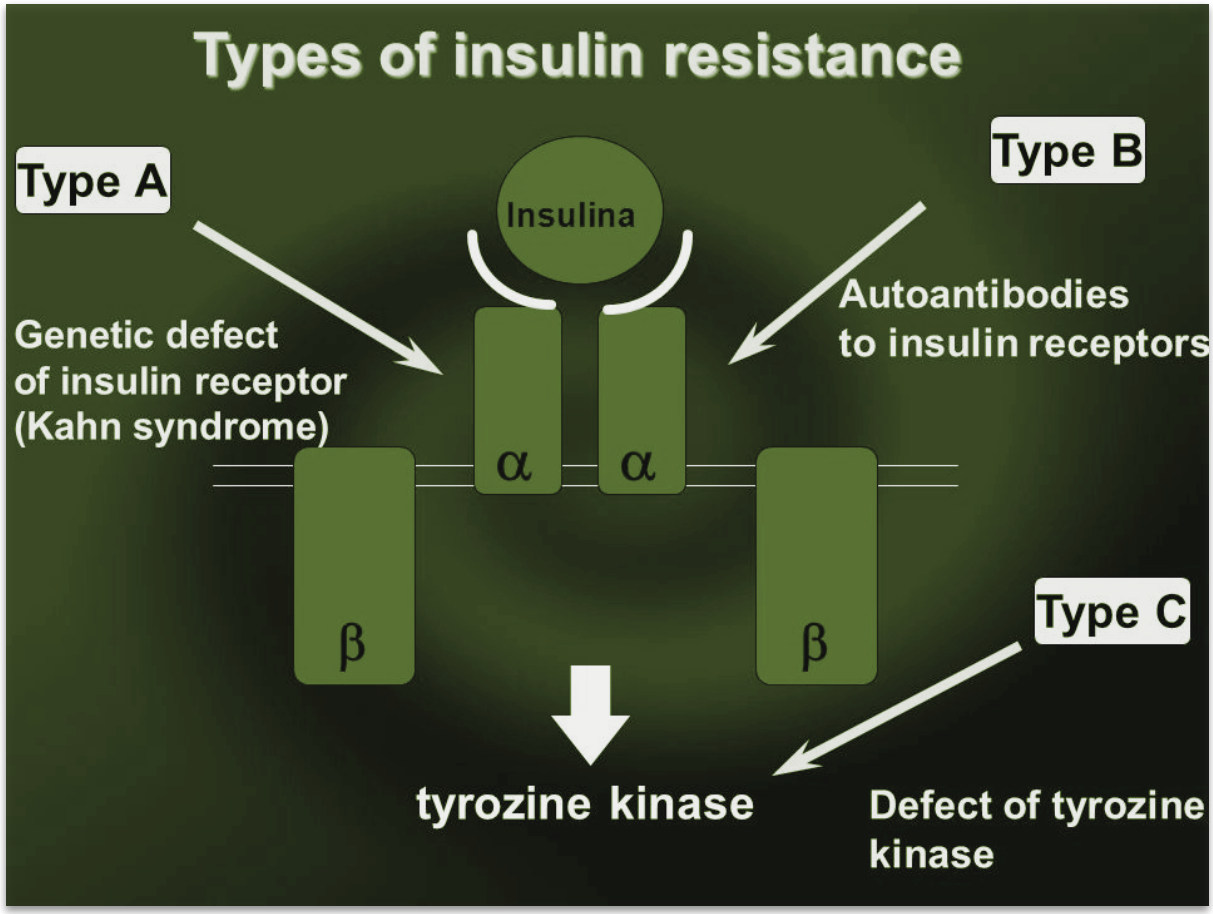
# IR Classification According To Receptor Site

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# Other Causes Of IR

- Chronic diseases such as **chronic liver disease**, **chronic kidney disease**, **Cushing disease**…etc
- Medications (glucocorticoids, cyclosporine, protease inhibitors…etc)
- Aging (theories about GLUT4)
  - High sodium intake (increases cortisol production)
  - Stress

# IR Type A and B

Differentiation is important in choosing treatment and handling associations

**Type A (receptor defect)**

- Usually normal weight or lean patients
- Adolescents and young females
- Hyperandrogenism (type C and exists in 3% of these women)
- Inherited forms
- Hypoglycemia could be the only sign in males

**Type B (anti-insulin antibodies)**

- It is an Autoimmune disease (ab against insulin receptors)
- Other autoimmune diseases usually present (e.g. systemic lupus, Hashimoto's, rheumatoid ds….etc)
- Overweight
- Episodes of hypoglycemia (ranges from mild shakes and lightheadedness to extreme forms) usually patients have low fasting blood sugar but high HbA1c

# Functional Approach In IR

- Dietary changes (e.g.Low GI and low Fructose diet)
- Balancing beneficial lipids and fatty acid
- Balancing carbohydrates to lower Triglycerides
- Supplements

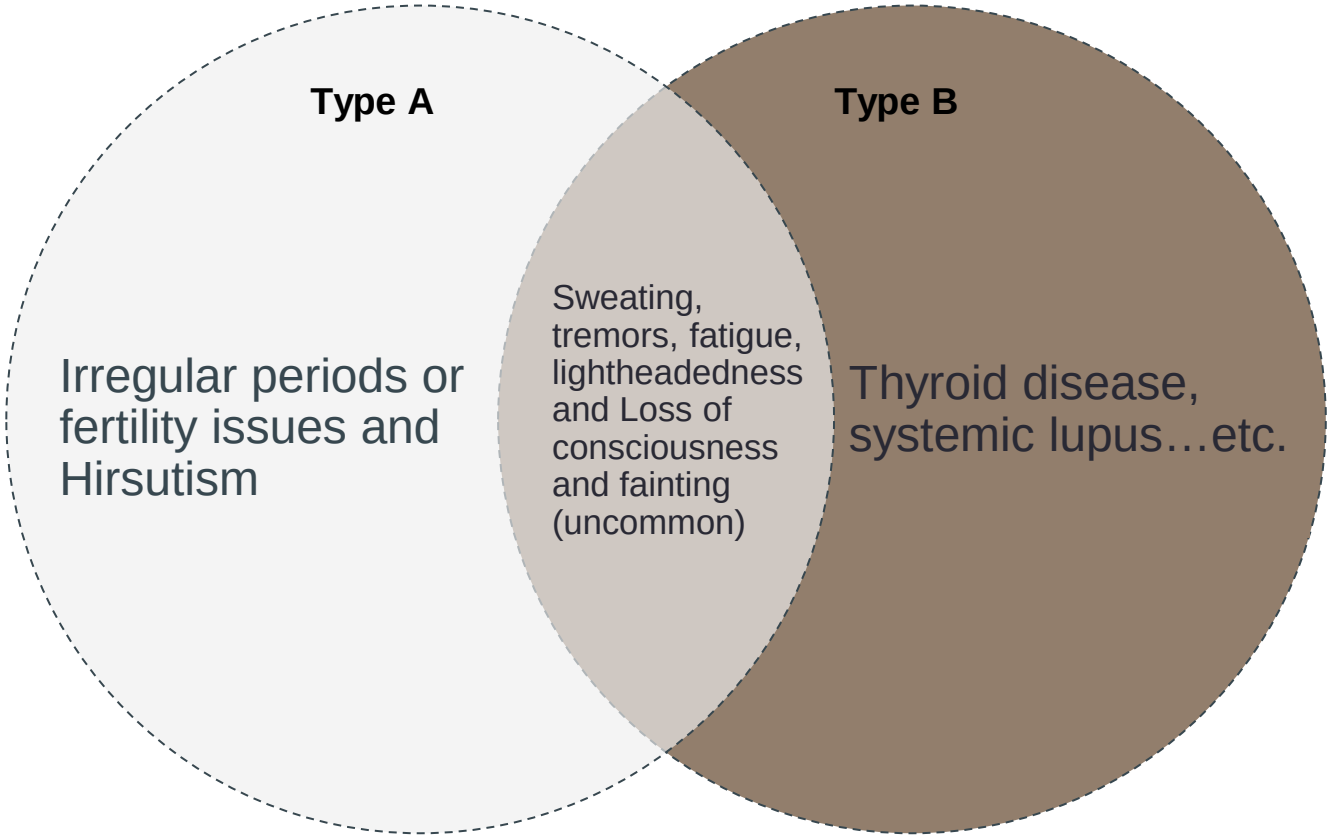
**This approach works on regular IR but not on Type A and Type B**

# Pitfalls In This Approach

- In Type A :
  - Pure focus on hyperandrogenism only
  - Mis-diagnosing and Treating it as PCOS only
  - Not diagnosing IR especially in lean patients

- In Type B:
  - Not checking for AI diseases or autoimmune process
  - Ignoring signs of hypoglycemia (especially in mild forms)
  - Treating overweight and IR as a regular case

# Differentiation and Its Importance (Clinical)

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# Differentiation and Its Importance (Lab)

**Type A**

- -ve antibodies against insulin receptors

- High androgen levels (free testosterone, DHEA-s)

- One or more equivocal +ve markers (ANA, Anti TPO antibodies….etc.)

**Type B**

- High HbA1c, low fasting or PP blood sugar

- Associated other autoimmune disease like hashimoto's or Lupus

- +ve antibodies against insulin receptors

- High Homa IR

- Moderate (20-50 mU/ml) to high levels of fasting insulin (>500mU/ml)

- Catabolic state in extreme cases (weight loss, ketosis)

# Case Presentation (Type A)

- 29 years old lady came to see me complaining of daily episodes of fatigue and brain fogginess, she can't tell If they are meal related. She also noticed more visible facial and body hair, her built was lean and she exercised regularly and is a vegetarian.

- She has regular menstrual history with occasional PMS , when asked about her most bothersome symptom she said that the episodes of sudden fatigue and weakness were affecting her quality of life the most.

# Case Presentation (Type A)

- **O/E**
  - she has a lean body built with a healthy body mass index, there was visible chest and facial hair (hirsutism). Skin pigmentation (acanthosis nigricans) at the nape of the neck.

- **Blood work:**
  - Normal CBC
  - High HbA1c 5.9%
  - Fasting blood sugar 65 mg/dl
  - Free testosterone 5pg/ml
  - Serum iron 34 ug/dl
  - Ferritin 15 ng/ml
  - Vitamin D3 5 ng/ml
  - HOMA IR was high
  - LH and FSH normal
  - Fasting insulin normal and PP was higher than 25

# Case Presentation (Type A)

- Pelvi- Abdominal U/S

  Normal with no cysts on the ovaries

- Home blood sugar monitoring and symptoms journaling was recommended and showed a pattern of low fasting and postprandial blood sugar but never below 65 mg/dl (this is important to exclude symptoms of insulinoma)

- Patient had criteria compatible with syndromes of hyperandrogenic insulin resistant either type A or C

# Case Presentation (Type A)

- Integrative approach
  - There is no consensus on treating Type A or C syndromes from evidence based standpoint

- We focused on treating insulin resistance through:
  - Low Glycemic index diet and proper meal planning
  - Low fructose diet (including fruits and juices)
  - Treat nutrient deficiency (Iron and vitamin D3 replacement)

# Case Presentation (Type A)

- **Treatment outcome:**
  - After 6 months of treating symptoms, with nutritional replacement and diet changes, labs normalized including HbA1c Testosterone and DHEA-s
  - The hypoglycemic attacks with the associated side effects became a rare occurrence

# Case Presentation (Type B)

- 45 years old male complaining of inability to lose weight (despite regular diet and exercise), attacks of sweating and tremors especially after meals, brain fogginess, low libido.

- Patient is known to have hypothyroidism and is on levothyroxine 100 mg/day since his early 20s, his thyroid function tests are all within normal range, he explains that he has always been on 50 mg/day but his primary provider increased it to 100 in attempt to help with the weight loss and fatigue but it didn't work.

# Case Presentation (Type B)

- He is active but drags himself to exercise and forces himself to focus at work

- His lifestyle is healthy and doesn't complain of stress but has interrupted sleep pattern

- **O/E**
  - Patient is overweight especially around the abdomen
  - He has sweaty and clammy skin
  - Blood pressure is normal
  - Cardiovascular and rest of systems is normal

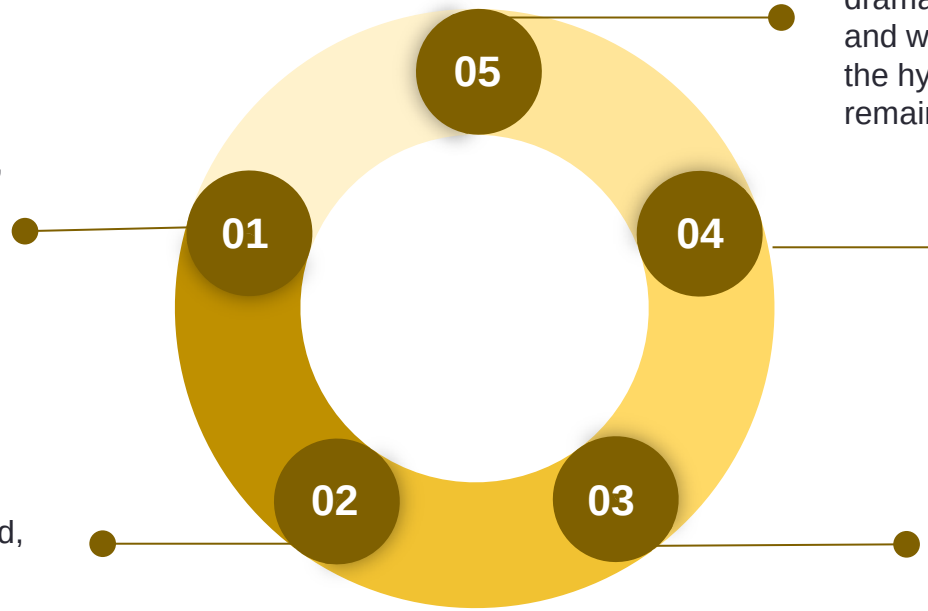
# Case Presentation (Type B)

- **Lab work**
  - HbA1c is 6.1%
  - Fasting blood sugar is 70 mg/dl
  - Lipid profile abnormal with prominent increase in TGS
  - CBC normal
  - CRP 5
  - Homocysteine 20
  - Vitamin D3 and Iron within normal range (optimum)
  - Thyroid function tests and hormone level normal
  - Adrenal assay normal

# Case Presentation (Type B)

- Lab work
  - Testosterone normal
  - Thyroid antibodies where >1000s range
  - Home blood sugar monitoring showed frequent hypoglycemia post meal
  - Stool analysis showed signs of leaky gut
  - HbA1c was in the prediabetes range

# Case presentation (Type B)




Thyroid antibodies dropped dramatically but sugar profile and weight issues along with the hypoglycemic attacks remained

Patient was health conscious, eats clean and regularly supplements (no major dietary changes made except for a Gluten free diet

Immune modulation through elimination of gluten and dairy and addition of selenium , vitamin A, vitamin C and probiotics was tried out for 3 months.

Chromium , alpha lipoic acid, acetyl cysteine was added

Melatonin and sleep journal was added (showed lack of REM sleep)

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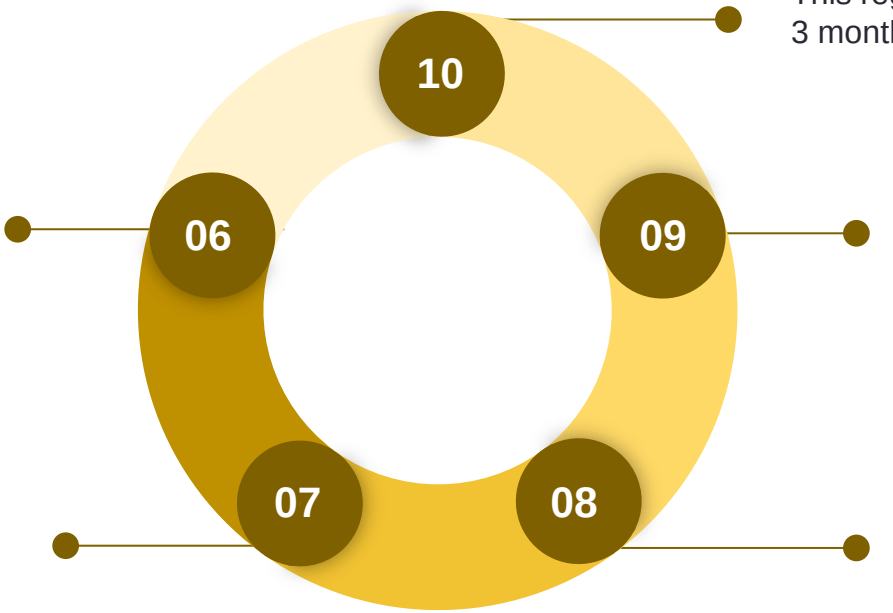
# Case Presentation (Type B)

This regimen was followed for 3 months

Due to the high homocysteine level (despite B12 supplementation ) and high LDL and TGs plus CRP, a trial of medication initiation was warranted




Daily turmeric,chromium and valerian and B12 supplementation

We started him on metformin 1000 mg/day

Added a statin with a co-Q10

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# Case Presentation (Type B)

- After 3 months Blood work normalized and medication cessation was implemented (statin and metformin)
- Patient  stayed on supplement for another 3 months
- More supplements removed and patient left with the basic daily ones (vitamin D3, probiotics, omega 3...etc)

# Treatment Type B

Integrative approach

Conventional approach

- Treating insulin resistance (**metformin**, liraglutide, thiazolidinediones, insulin)
- Treating immune process (immunosuppressant and immunomodulatory)
- Treating hyperlipidemia and metabolic syndrome
-Weight loss

**- Supplements for IR and inflammation**

- Vitamin C 1000 mg/day
- Chromium 1000 mg/day
- Magnesium 400 mg/day
- Alpha lipoic acid 600 mg/day

**- Supplements for immune system support**

- Echinacea 100 mg/day
- Vitamin A 10,000 IU/day
- Vitamin D 5,000 IU/day
- Probiotics 50 billion combination Strain

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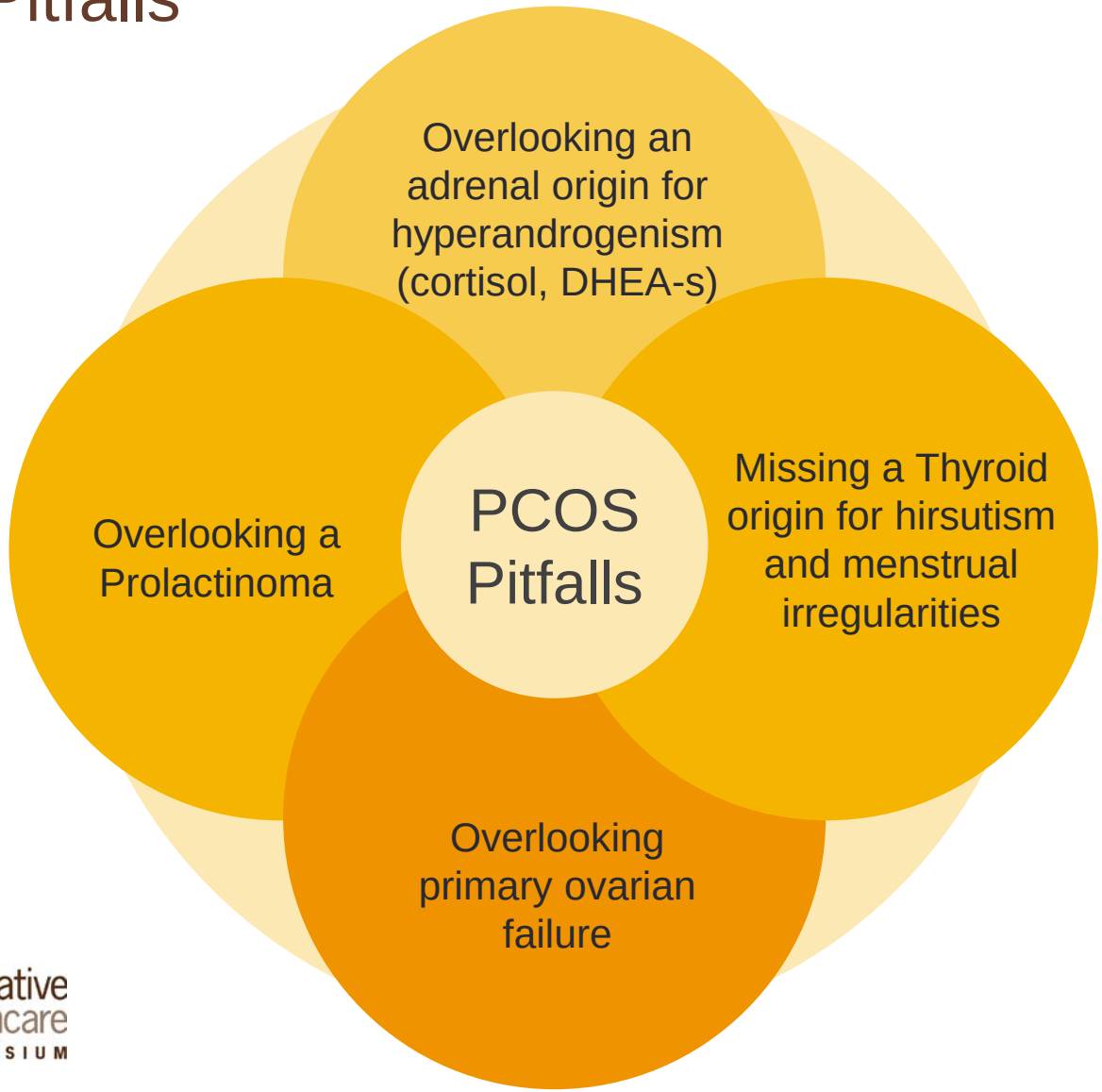
# PCOS

- PCOS is characterized by menstrual irregularities, anovulation and signs of hyperandrogenism.
- Resulting from a dysfunction in the HPA-Axis
- Associated with DM, Infertility, obesity and metabolic syndrome and sleep apnea
- Rotterdam criteria

# PCOS

- Free testosterone level
- Hormonal assay including TSH, HCG, prolactin, FSH and LH including ratio
- Glucose, fasting insulin or HOMA IR and metabolic profile
- Ultrasound

# PCOS Pitfalls

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# Integrative approach

Look for: signs of inflammation and nutrients deficiencies and whether this is just a biochemical diagnosis versus an ultrasound diagnosis.

**Integrative Treatment**

- Treatment of metabolic derangements
- Treat insulin resistance (metformin, low GI, chromium, magnesium and Alpha lipoic acid)
- Treat inflammation in metabolic syndrome ( anti inflammatory diet, vitamin D3 supplementation, vitamin C)

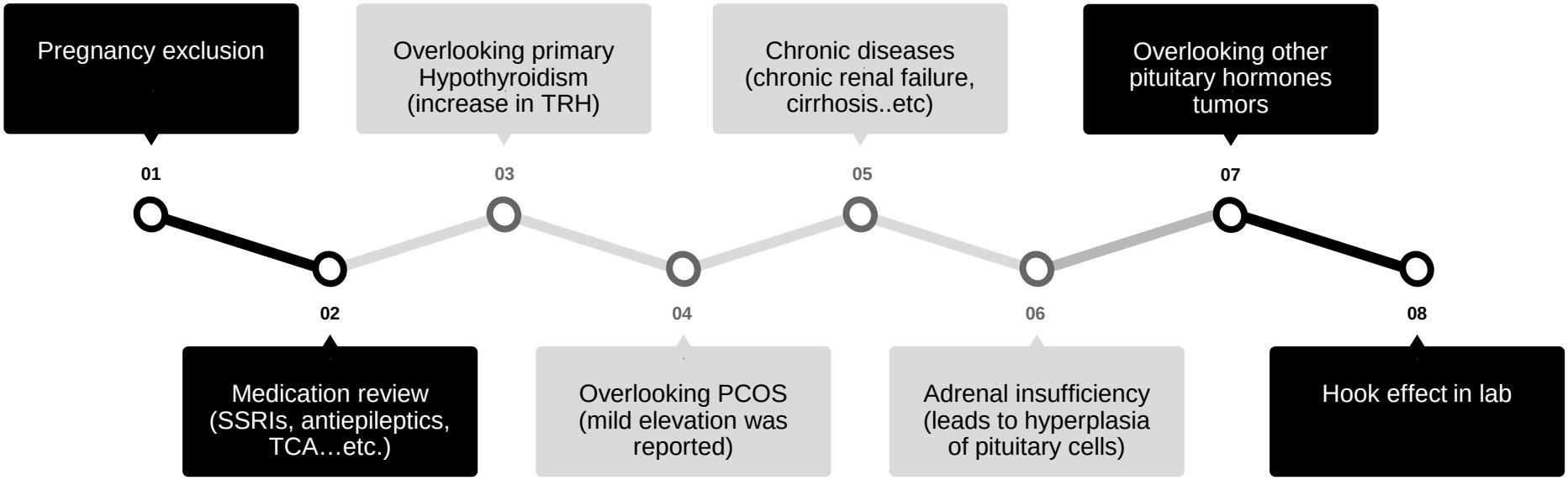
# Prolactinoma

- **Incidence:**
  - Most common hormone-secreting pituitary tumors
  - Female: male incidence is 10:1
  - Prevalence not known globally but in the U.S. 6-25% of population has pituitary tumors on autopsy

# Prolactinoma

- **Clinical Presentation:**
  - Hormonal effect:
    - Amenorrhea or menstrual irregularities
    - Galactorrhea
    - Osteopenia or osteoporosis
    - Decreased libido and erectile dysfunction in males
  - Pressure effects:
    - Deficiencies in one or more of (TSH, GH, ACTH)
    - Headaches
    - Visual problems

# Prolactinoma Pitfall and proper diagnosis

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# Management

- **Diagnosis:**
  - Prolactin levels on one or more occasions especially if the levels are only mildly elevated
  - Pregnancy test
  - TSH and thyroid functions (TRH is a PRF)
  - Adrenal function tests including ACTH
  - Exclude other causes of high prolactin
  - MRI
- **Treatment:**
  - Management according to MRI either medical or surgical

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  - Aug 28, 2017 Author: Richard Scott Lucidi, MD, FACOG; Chief Editor: Richard Scott Lucidi, MD


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