

Inositols for PCOS : An Update

Mark H. Ratner, MD
Shady Grove Reproductive Science Center
Rockville, Maryland

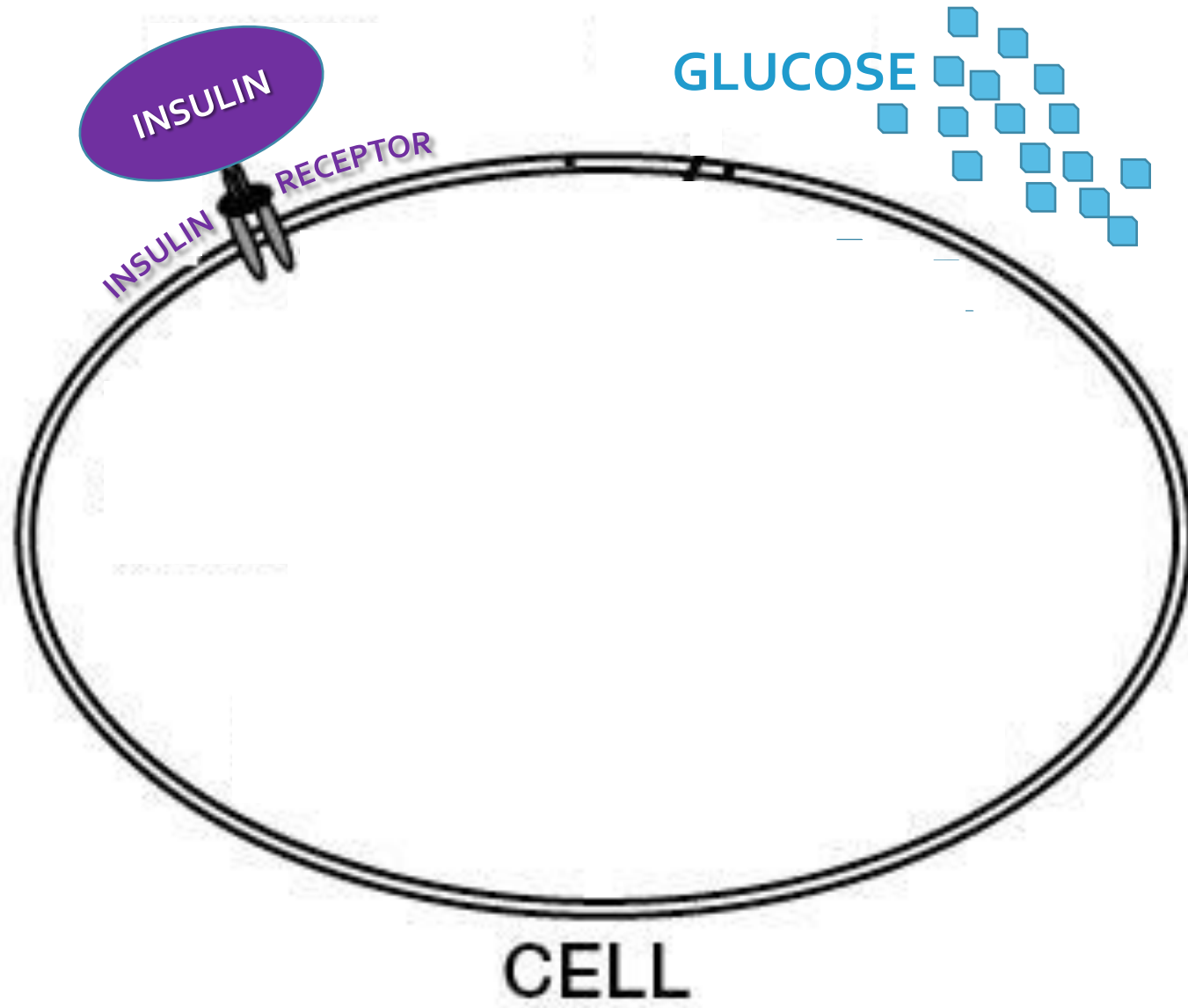
Overview

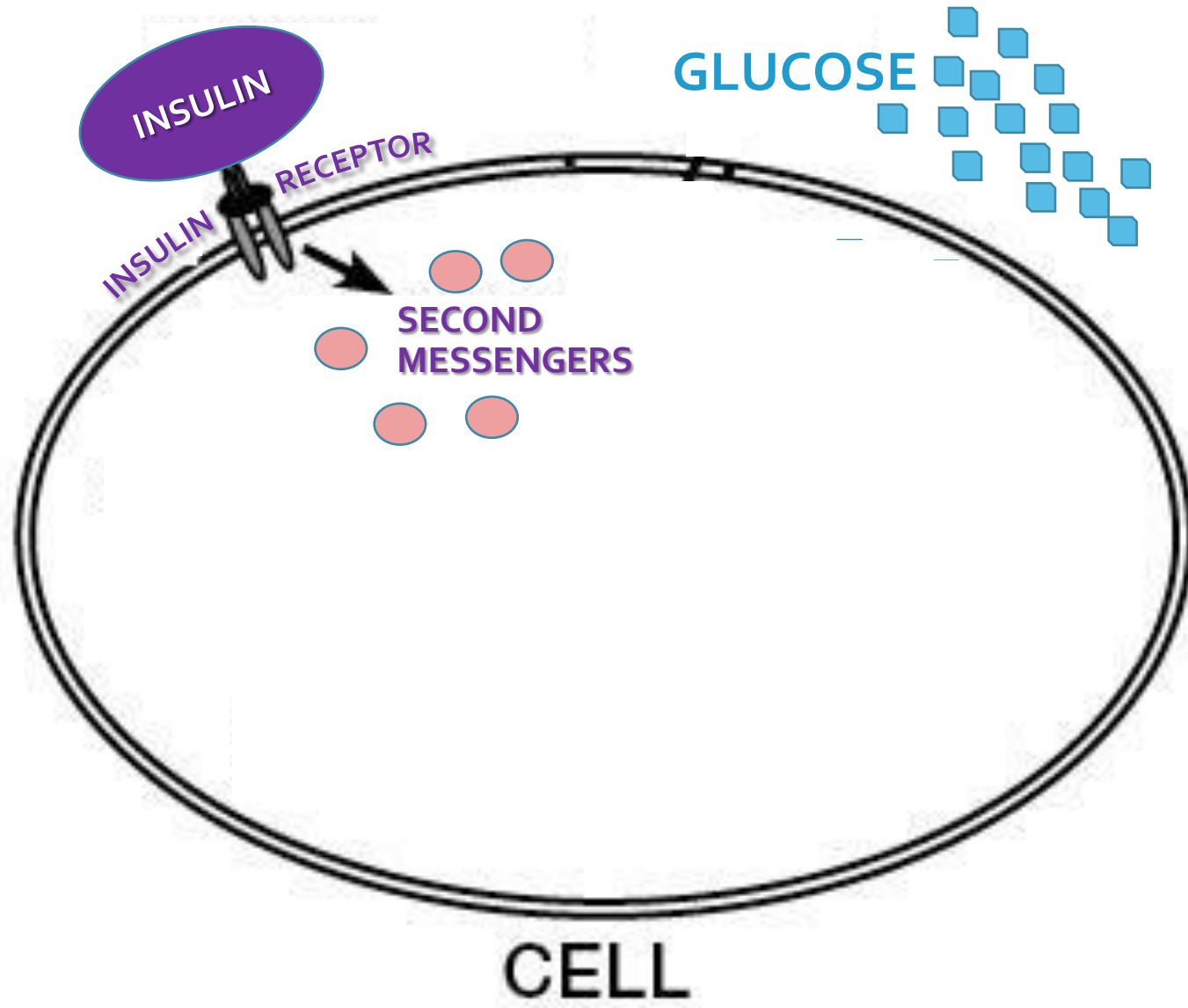
- Understanding the role of insulin in PCOS
- The relationship between inositols and insulin
- Inositols for PCOS : Published studies
- Practical considerations

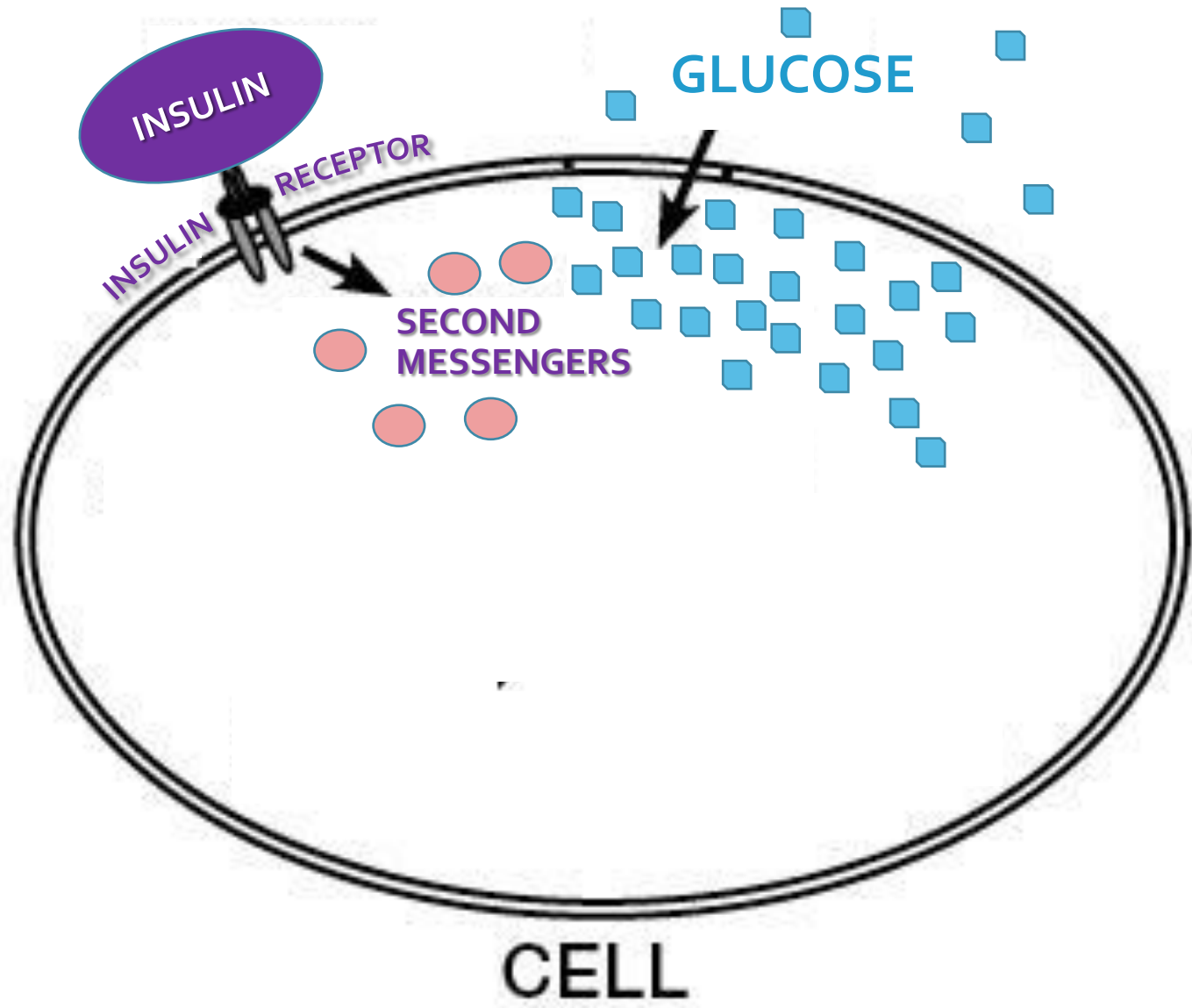
Understanding the role of insulin

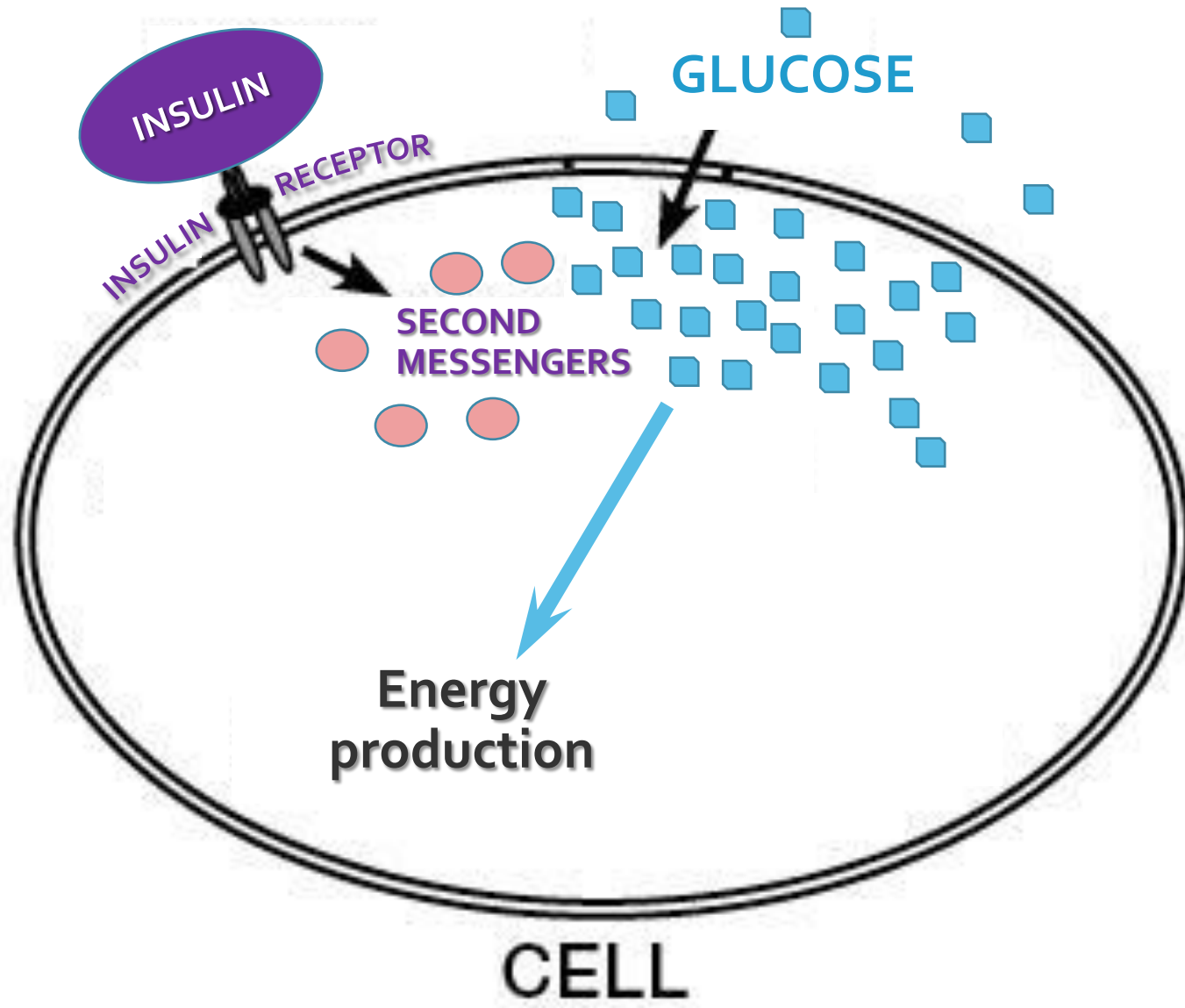
Understanding the role of insulin

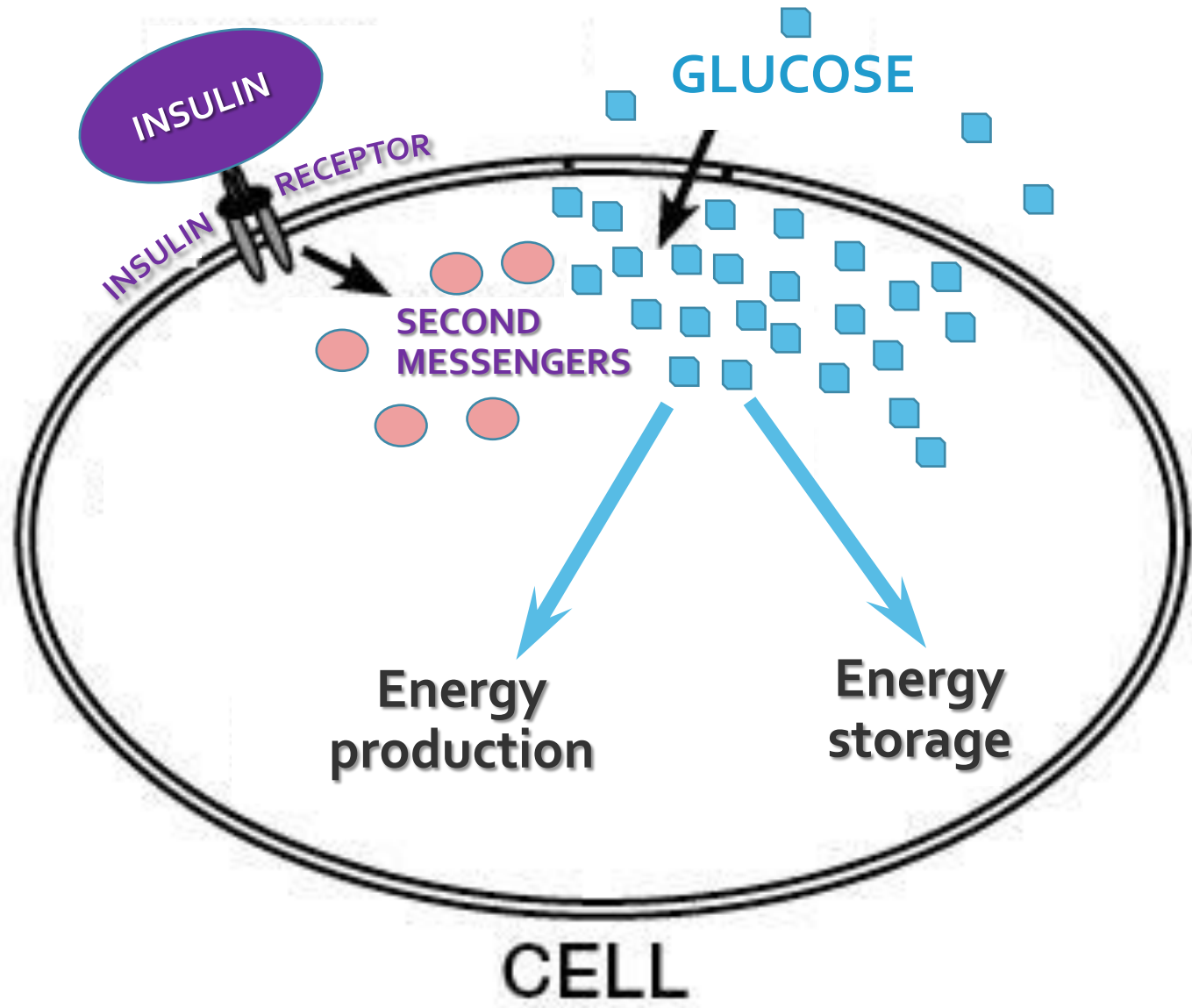
- A hormone produced by the pancreas that regulates glucose metabolism



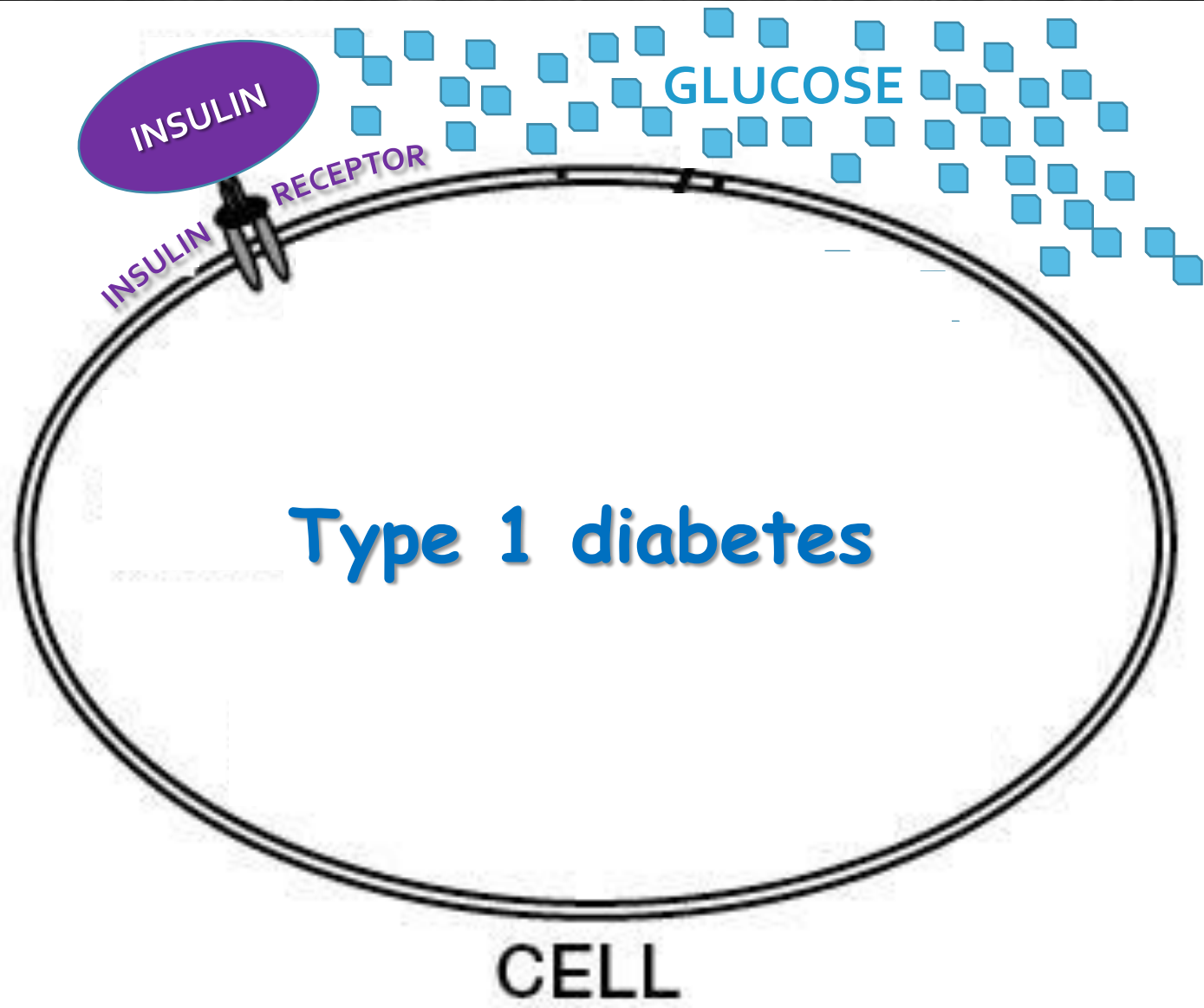


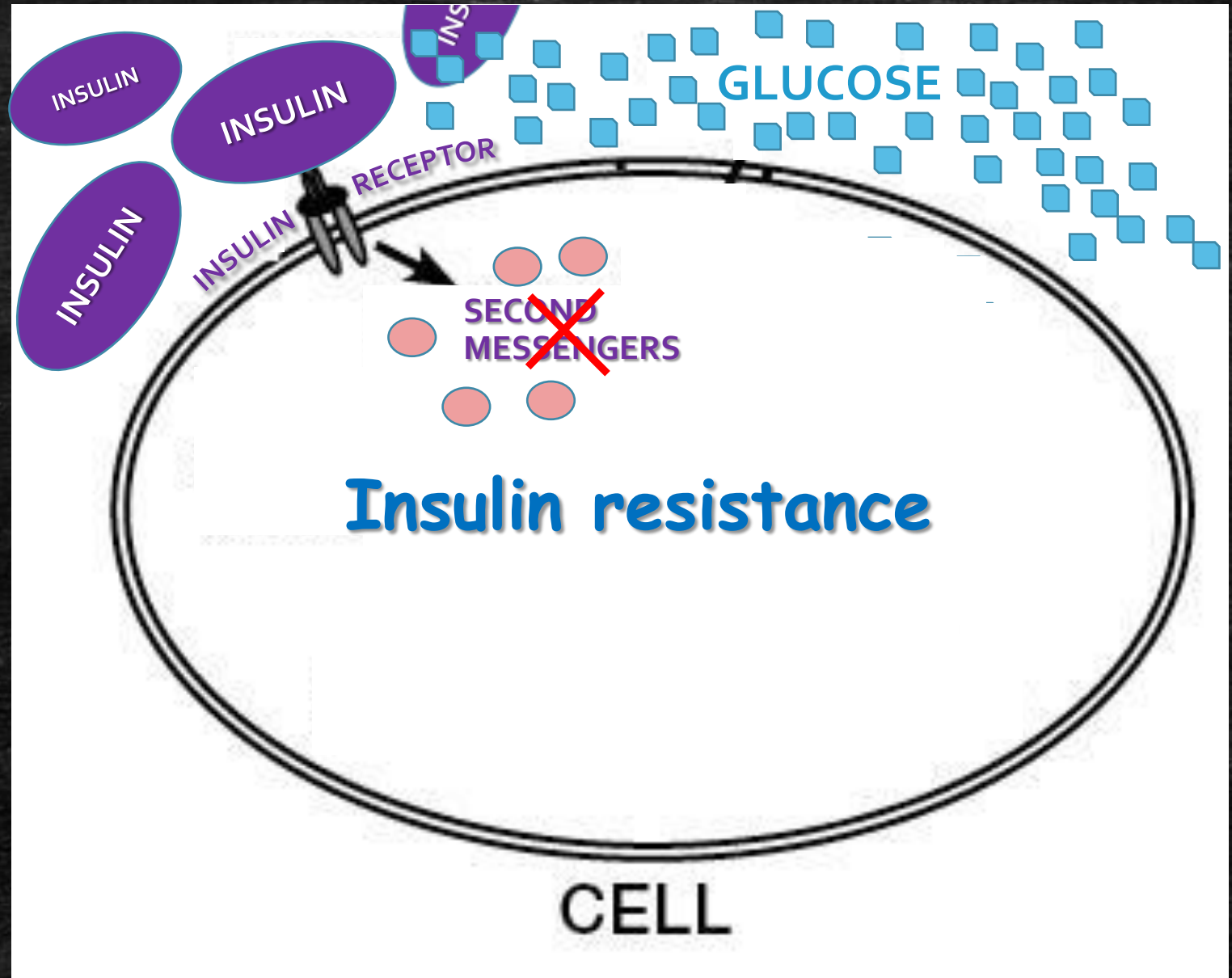






So, what can go wrong??





Understanding the role of insulin

- A hormone produced by the pancreas that regulates glucose metabolism
- Insulin resistance (IR) is present in 70-80% of women with PCOS
 - Increased blood sugar ("hyperglycemia")
 - Increased serum insulin levels ("hyperinsulinemia")
- Increased serum insulin levels then cause the ovary to produce increased amounts of testosterone
- Increased serum insulin and testosterone interfere with ovulation

Metformin and PCOS

Metformin and PCOS

- Metformin is an insulin sensitizing drug
- Improves function of second messengers, and reduces insulin resistance
- Reduces hyperinsulinemia and testosterone overproduction
- Common side effects:
 - Bloating
 - Nausea
 - Diarrhea
 - Loss of appetite

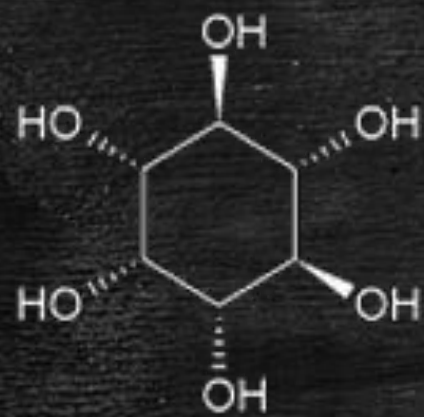
Overview

- Understanding the role of insulin in PCOS
- The relationship between inositols and insulin
- Inositol for PCOS : Published studies
- Practical considerations

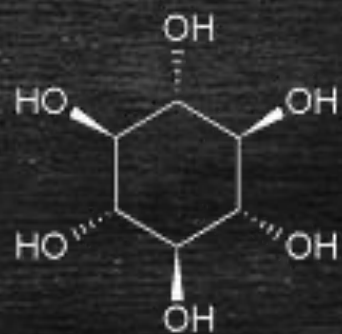
Inositols

Inositols

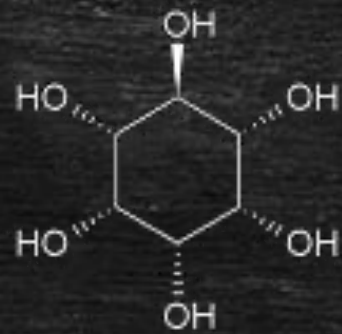
- 6-carbon sugars - similar to mannitol and sorbitol
- 9 different types of inositols - "stereoisomers"



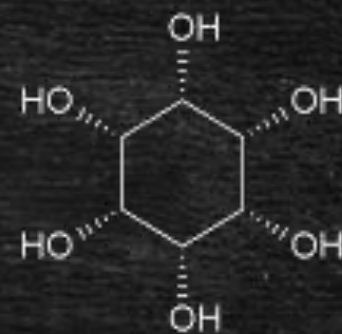
Myo-Inositol



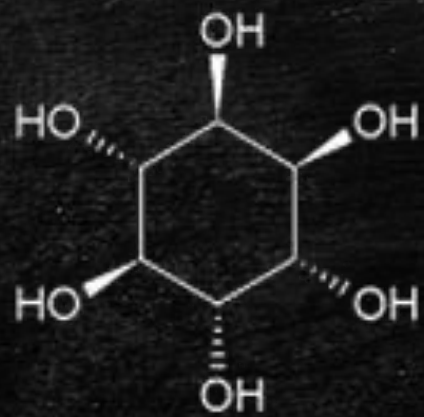
Scyllo-Inositol



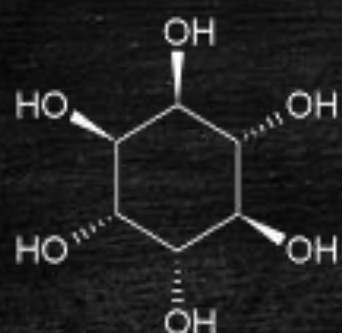
Epi-Inositol



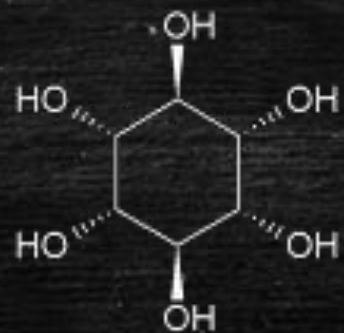
Cis-Inositol



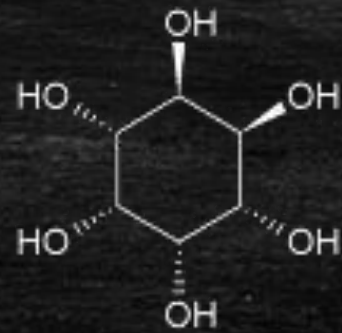
D-chiro-Inositol



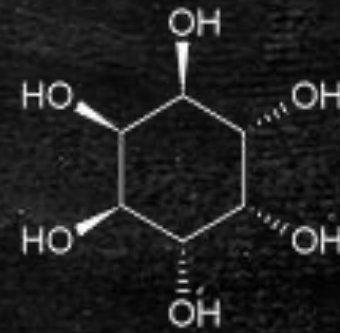
L-Chiro-Inositol



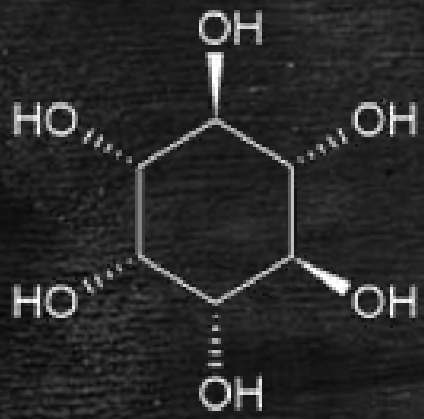
Muco-Inositol



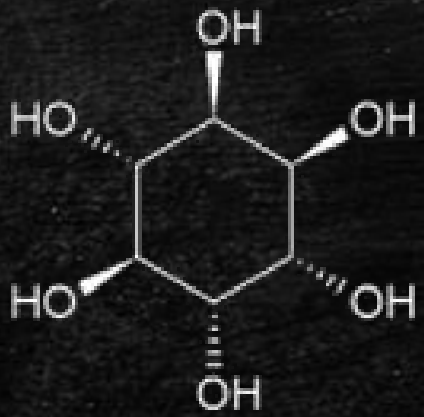
Allo-Inositol



Neo-Inositol



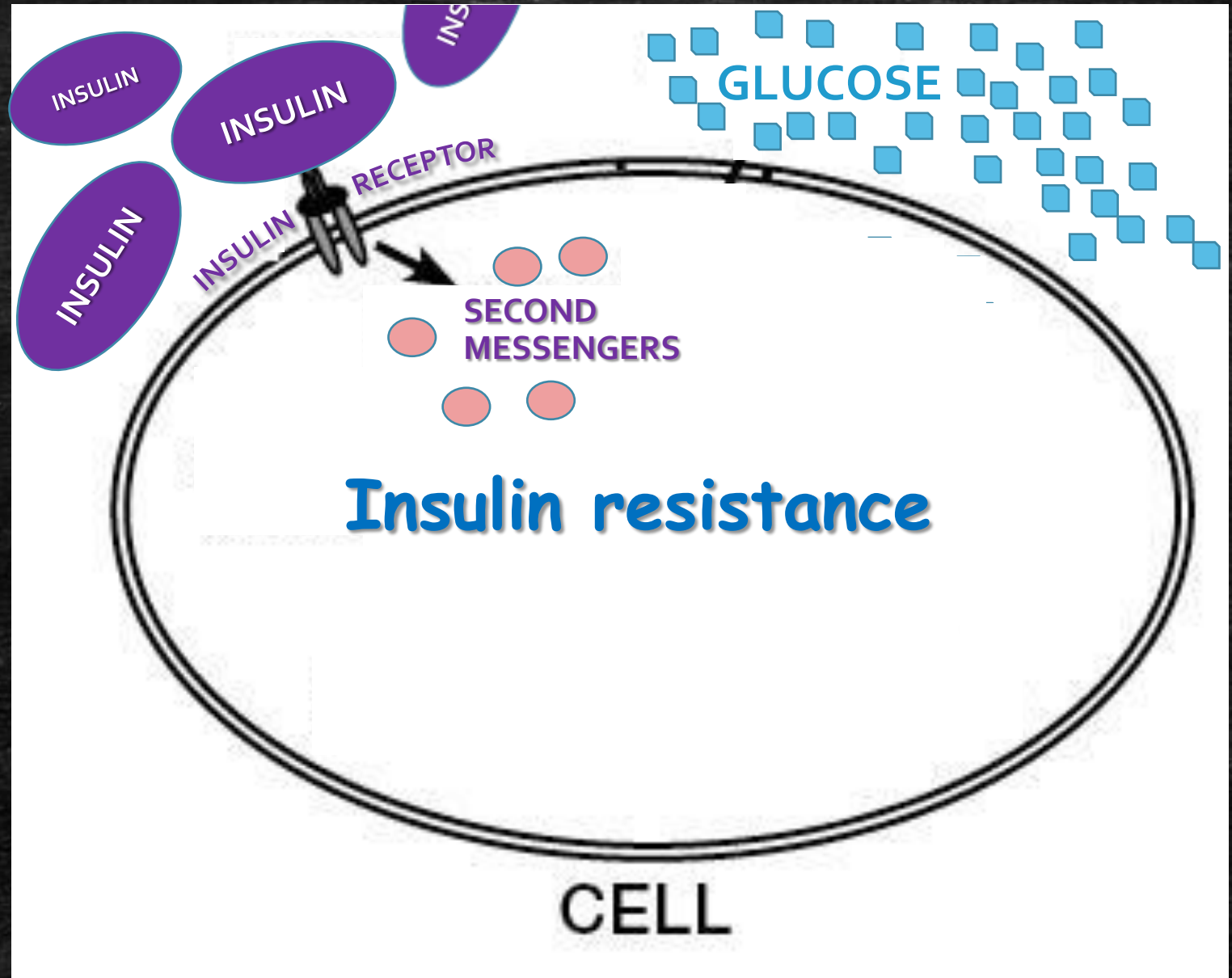
Myo-Inositol

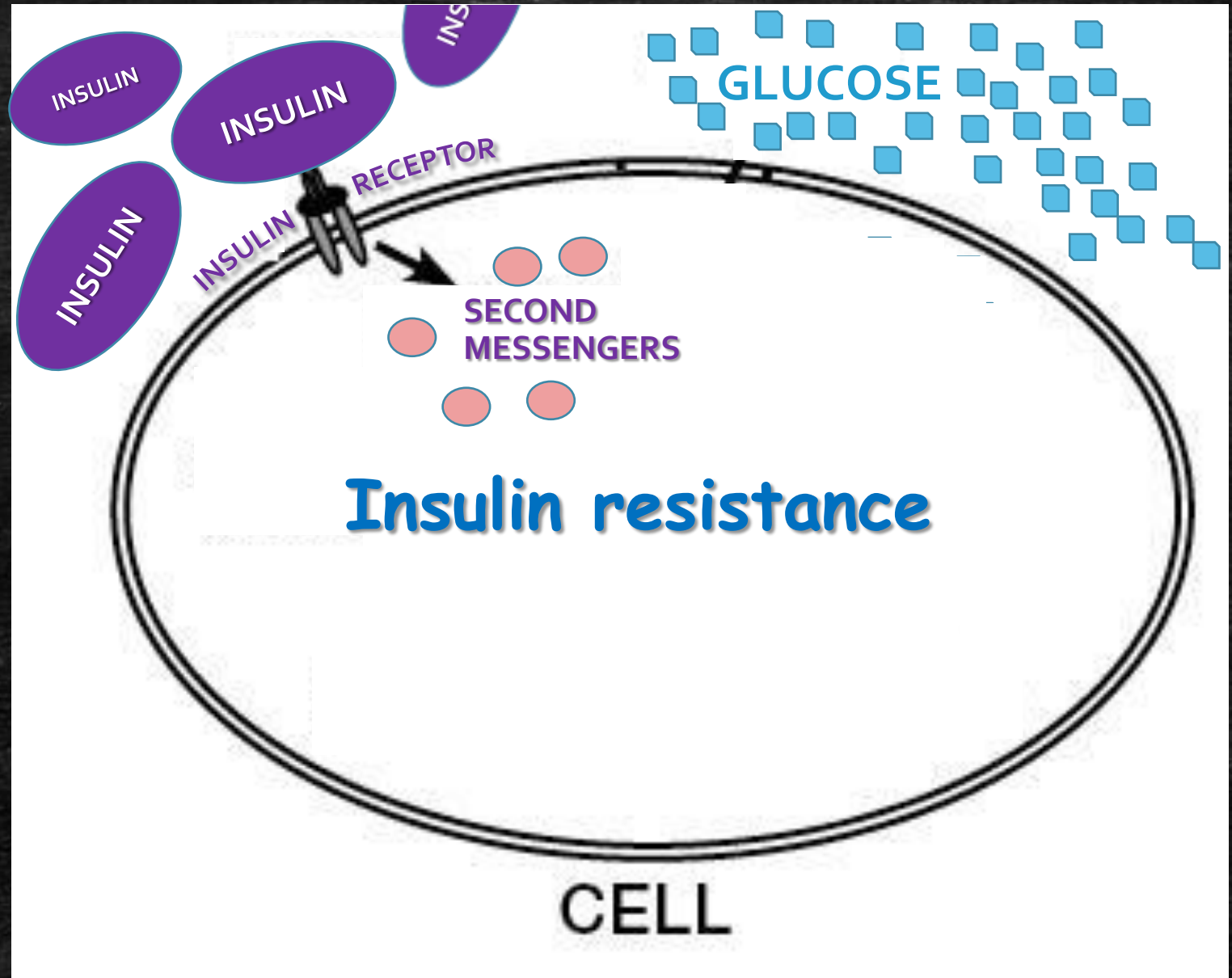


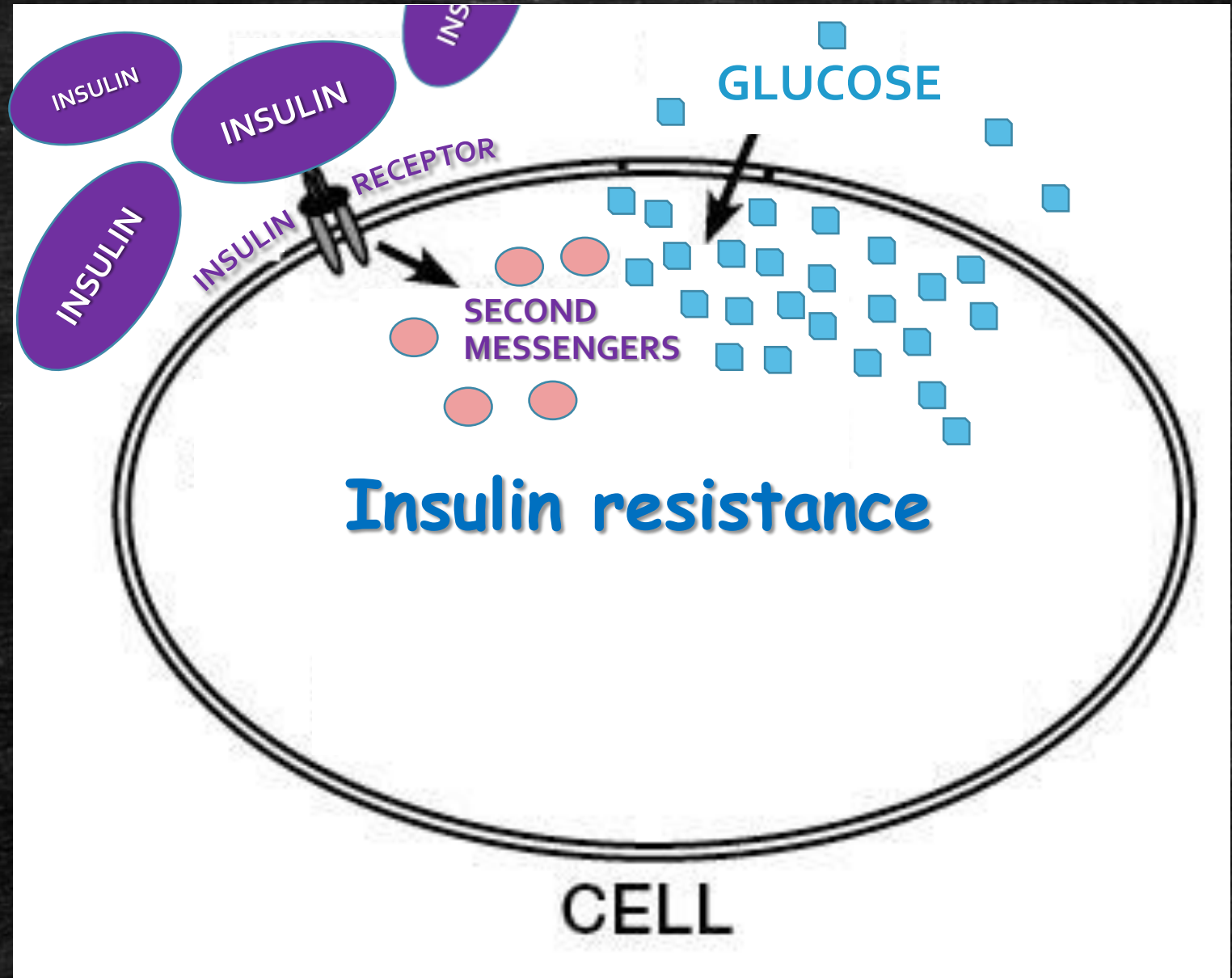
D-chiro-Inositol

Inositols

- 6-carbon sugars - similar to mannitol and sorbitol
- 9 different types of inositols - "stereoisomers"
- *Myo-inositol (MYO)* and *d-chiro inositol (DCI)* are key components of the "second messengers"







Inositols

- 6-carbon sugars - similar to mannitol and sorbitol
- 9 different types of inositols - "stereoisomers"
- The insulin receptor's "second messengers" contain *myo-inositol (MYO)* and *d-chiro inositol (DCI)*
- Supplementing with MYO and DCI will improve insulin receptor "signaling" and reduce insulin resistance
- First inositol/PCOS clinical trial published in 1999 by Nestler, et al, using DCI alone

Overview

- Understanding the role of insulin in PCOS
- The relationship between inositols and insulin
- Inositol for PCOS : Published studies
- Practical considerations

Zacche MM, et al, "*Efficacy of myo-inositol in the treatment of cutaneous disorders in young women with PCOS*", *Gynecol Endocrinology*, 2009, 25:8, 508-13

- 50 women with PCOS
- Treated with 4 g MYO for 3 months

Zacche MM, et al, "*Efficacy of myo-inositol in the treatment of cutaneous disorders in young women with PCOS*", *Gynecol Endocrinology*, 2009, 25:8, 508-13

- 50 women with PCOS
- Treated with 4 g MYO for 3 months
- Testosterone decreased 30% w/ MYO treatment (p=.001)
- Insulin resistance decreased 50% (p=.005)

Zacche MM, et al, "*Efficacy of myo-inositol in the treatment of cutaneous disorders in young women with PCOS*", *Gynecol Endocrinology*, 2009, 25:8, 508-13

- 50 women with PCOS
- Treated with 4 g MYO for 3 months
- Testosterone decreased 30% w/ MYO treatment (p=.001)
- Insulin resistance decreased 50% (p=.005)
- 30% of patients had disappearance of hirsutism
- 53% of patients had resolution of acne

Minozzi, et al, "*The effect of a combination therapy with myo-inositol and a combined oral contraceptive pill vs. a combination oral contraceptive pill alone on metabolic, endocrine and clinical parameters in PCOS*", *Gyn Endoc*, 2011, 27:11, 920-924

- 155 women with PCOS
- Randomized to treatment with either BCP+MYO or BCP alone

Minozzi, et al, "The effect of a combination therapy with myo-inositol and a combined oral contraceptive pill vs. a combination oral contraceptive pill alone on metabolic, endocrine and clinical parameters in PCOS", Gyn Endoc, 2011, 27:11, 920-924

- 155 women with PCOS
- Randomized to treatment with either BCP+MYO or BCP alone

	Birth Control Pill	Birth Control Pill + Myo-inositol	
Reduction in testosterone	29%	44%	P<.05
Reduction in insulin resistance	7%	38%	P<.05

Costantino, et al, "*Metabolic and hormonal effects of myo-inositol in women with PCOS: a double blind trial*", Eur Rev Med Pharmacol Sci, 2009, 13:2, 105-10

- 42 women with PCOS
- Randomized to either 4 grams MYO daily or placebo

Costantino, et al, "*Metabolic and hormonal effects of myo-inositol in women with PCOS: a double blind trial*", Eur Rev Med Pharmacol Sci, 2009, 13:2, 105-10

- 42 women with PCOS
- Randomized to either 4 grams MYO daily or placebo
- Testosterone decreased 65% in MYO group (p=.003)
- Insulin sensitivity increased 80% in MYO group (p=.001)

Costantino, et al, "*Metabolic and hormonal effects of myo-inositol in women with PCOS: a double blind trial*", Eur Rev Med Pharmacol Sci, 2009, 13:2, 105-10

- 42 women with PCOS
- Randomized to either 4 grams MYO daily or placebo
- Testosterone decreased 65% in MYO group (p=.003)
- Insulin sensitivity increased 80% in MYO group (p=.001)
- 70% of subjects in MYO group ovulated during study, compared to 21% in the placebo group

Raffone, et al, "*Insulin sensitizer agents alone and in co-treatment with r-FSH for ovulation induction in PCOS women*", *Gynecol Endocrinology*, 2010, 26:4, 275-80

- 120 women with PCOS and chronic anovulation
- Randomized to treatment with either metformin or myo-inositol

Raffone, et al, "Insulin sensitizer agents alone and in co-treatment with r-FSH for ovulation induction in PCOS women", *Gynecol Endocrinology*, 2010, 26:4, 275-80

- 120 women with PCOS and chronic anovulation
- Randomized to treatment with either metformin or myo-inositol

	Ovulation rate	Pregnancy rate
Metformin	50%	18%
Myo-inositol	65%	30%

Raffone, et al, "Insulin sensitizer agents alone and in co-treatment with r-FSH for ovulation induction in PCOS women", *Gynecol Endocrinology*, 2010, 26:4, 275-80

- 120 women with PCOS and chronic anovulation
- Randomized to treatment with either metformin or myo-inositol

	Ovulation rate	Pregnancy rate
Metformin	50%	18%
Myo-inositol	65%	30%
Clomiphene (Legro, 2014)	48%	19%

Raffone, et al, "Insulin sensitizer agents alone and in co-treatment with r-FSH for ovulation induction in PCOS women", *Gynecol Endocrinology*, 2010, 26:4, 275-80

- 120 women with PCOS and chronic anovulation
- Randomized to treatment with either metformin or myo-inositol

	Ovulation rate	Pregnancy rate
Metformin	50%	18%
Myo-inositol	65%	30%
Clomiphene (Legro, 2014)	48%	19%
Letrozole (Legro, 2014)	62%	28%

Colazingari, et al, "The combined therapy MYO plus DCI, rather than DCI, is able to improve IVF outcomes: results from a randomized controlled trial", Arch Gyn Obstet, 2013, 288: 1405-1411

- 100 women with PCOS and undergoing IVF
- Randomized to treatment with either MYO+DCI, or, DCI alone
- Combined treatment group had better embryo quality and higher fertilization and pregnancy rate

MYO and DCI play different roles

- MYO and DCI are both inositols, but are VERY different molecules
- Each produces a different second messenger
- MYO improves ovarian function
- DCI improves metabolic function in the peripheral tissues
- Combined treatment with MYO and "low-dose" DCI together appears to be more effective than either alone

Inositols for PCOS: Practical Concerns

- The combination of myo-inositol and d-chiro inositol is an effective treatment for PCOS
 - 2-4 grams of MYO/day
 - 50-100 mg of DCI/day
- Safe, inexpensive and completely free of side effects
- Available without prescription, as OTC dietary supplements

Questions?