

Riding the Waves of Obesity Science

A MULTI-PATHWAY RATIONALE FOR THE NEXT THERAPEUTIC CURRENT

| Why the next era of obesity care won't be built on a single pathway.

CME OUTFITTERS 

More than 40% of U.S. adults live with obesity, and incretin-based therapies have reset expectations for what treatment can achieve. Yet one question sets the stage for everything that follows in this series: if no single mechanism drives obesity in every patient, why would we expect one mechanism to treat it? In this opening conversation, **Lee M. Kaplan, MD, PhD**, joins series chair **Robert F. Kushner, MD**, to frame obesity as a chronic, relapsing disease whose defining feature is heterogeneity — and to make the clinical case for a multi-pathway future.

KEY CONCEPTS

- **One disease, many drivers.** Obesity is a chronic, relapsing pathophysiologic disorder. Because no single pathway causes it, no single pathway will control it across the whole population.
- **The ceiling of single-pathway therapy.** Even highly effective single-mechanism treatment leaves residual, population-level unmet need — much as some patients normalize on one antihypertensive while others need three or four.
- **Adding a mechanism, not just amplifying one.** A second pathway can do more than give everyone the same extra increment — it can preferentially help the patients who responded poorly to the first, so the two mechanisms cover each other's gaps. The patient who gains little on drug A may be exactly the one who benefits from adding drug B.

“THE SNACK” INFO BOX

FORMAT	30 min video CME “Snack” — a moderated expert conversation
FACULTY	Lee M. Kaplan, MD, PhD, with chair Robert F. Kushner, MD
AUDIENCE	Obesity-medicine, endocrinology, primary care & cardiometabolic clinicians (MD, NP, PA, PharmD)

LEARNING OBJECTIVE

Identify obesity as a chronic, relapsing disease process with unmet needs that motivate multi-pathway therapeutic development.

THE SERIES AHEAD — FOUR SNACKS, ONE ARC 4 EXPERTS, 1 RENOWNED CHAIR

SNACK ONE (NOW)

The multi-pathway rationale
Lee M. Kaplan, MD, PhD

SNACK TWO

The biology of amylin
Matthew R. Hayes, PhD

SNACK THREE

Phenotypes & who benefits
Andres Acosta, MD, PhD

SNACK FOUR

Emerging therapies & the data
W. Timothy Garvey, MD

Chaired throughout by **Robert F. Kushner, MD** — Northwestern University
Feinberg School of Medicine

A NOTE ON DURABILITY

Weight regain is seen when effective treatment is stopped — much like glycemic control worsening after diabetes medication is discontinued — not during continued therapy. The case for staying on treatment is a case about biology, not willpower.

“There isn’t one single pathway that causes obesity, and there won’t be one single pathway that ends it — or controls it — in all people.”

— Lee M. Kaplan, MD, PhD

DIRECTOR, OBESITY, METABOLISM & NUTRITION INSTITUTE
BOSTON, MA

LOOKING AHEAD — THE AMYLIN CURRENT

Enter amylin — a physiologic satiety hormone acting through brain pathways distinct from, and complementary to, the incretins. Because they engage different targets, emerging amylin-based therapies are a genuinely new “current” — the multi-pathway logic this series explores, in practice.

Emerging amylin agents are investigational; efficacy and safety data are presented as such — fair-balanced and evidence-based — in later Snacks in the series.

SUGGESTED READING

Kaplan LM, Apovian CM, Ard JD, et al. Assessing the state of obesity care: quality, access, guidelines, and standards. *Obes Sci Pract.* 2024;10(4):e765.

Volcansek S, Koceva A, Jensterle M, et al. Amylin: from mode of action to future clinical potential in diabetes and obesity. *Diabetes Ther.* 2025;16(6):1207-1227.

Garvey WT, Blüher M, Osorio Contreras CK, et al. Coadministered cagrilintide and semaglutide in adults with overweight or obesity. *N Engl J Med.* 2025;393(7):635-647.

Acosta A, Camilleri M, Abu Dayyeh B, et al. Selection of antiobesity medications based on phenotypes enhances weight loss: a pragmatic trial. *Obesity (Silver Spring).* 2021;29(4):662-671.

ACCREDITATION & SUPPORT

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