

New strategies in management of childhood obesity



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Outline

- Introduction to obesity epidemics worldwide.
- Escalating rates of pediatric obesity.
- Prevention is main role in management of Pediatric obesity.
- Various strategies in management of Pediatric obesity.
 - Dietary changes into healthy diet.
 - Rule of High fiber diet on gut microbiota
 - Pre/Probiotics use in obesity.
 - Exercise.
 - Behavioral changes.
- New medications available to treat obesity in adults
- Surgical Approach to adolescent obesity.

Background

- Obesity & overweight among children & adolescents is increasing at an alarming rate, which lead to the increase in the incidence of their related co-morbidities.
- In the meantime, rates of obesity continue to increase, especially in low income children.
- Despite the highest rates of childhood obesity worldwide over the last 30 years, there is still **no clear treatment strategy**.
- A great deal of the research effort into solving the problem of childhood obesity is directed **toward prevention through efforts to modify the family's dietary and lifestyle habits**.

- If not prevented or treated, these children will suffer from psychosocial issues (e.g., depression, being bullied, & decreased school performance) & Physical complications (e.g., hypertension, nonalcoholic fatty liver disease, type 2 diabetes, hyperlipidemia & ultimately metabolic syndrome).
- Newer medications have come onto the market for the treatment of adults with obesity, but **none of these newer medications** are currently FDA approved for use in children with obesity.
- Bariatric surgery, while being done more frequently in adolescents, is still reserved for adolescents with severe obesity, and is best accomplished in a center with expertise.

Rising Rate of Childhood
Overweight & Obesity is
ALARMING!

LACK OF PHYSICAL EXERCISE AND UNHEALTHY FOOD CHOICES



Approximately 1 every 4 children in the United States is considered overweight



Prevalence of overweight & obesity in Saudi children & adolescents

Mohammad I. El Mouzan,^a Peter J. Foster,^b Abdullah S. Al Herbish,^a
Abdullah A. Al Salloum,^a Ahmad A. Al Omer,^c Mansour M. Qurachi,^d
and Tatjana Kecojevic^b

–***Ann Saudi Med.* 2010 May–Jun;3(30)**
208–203

- The national sample size, in Saudi reference was 19 317 healthy children & adolescents from 5 - 18 years of age
- The prevalence of **overweight 23.1%, obesity & %9.3severe obesity,%2**in all age groups

Prevention strategies is the rule in Pediatric Obesity

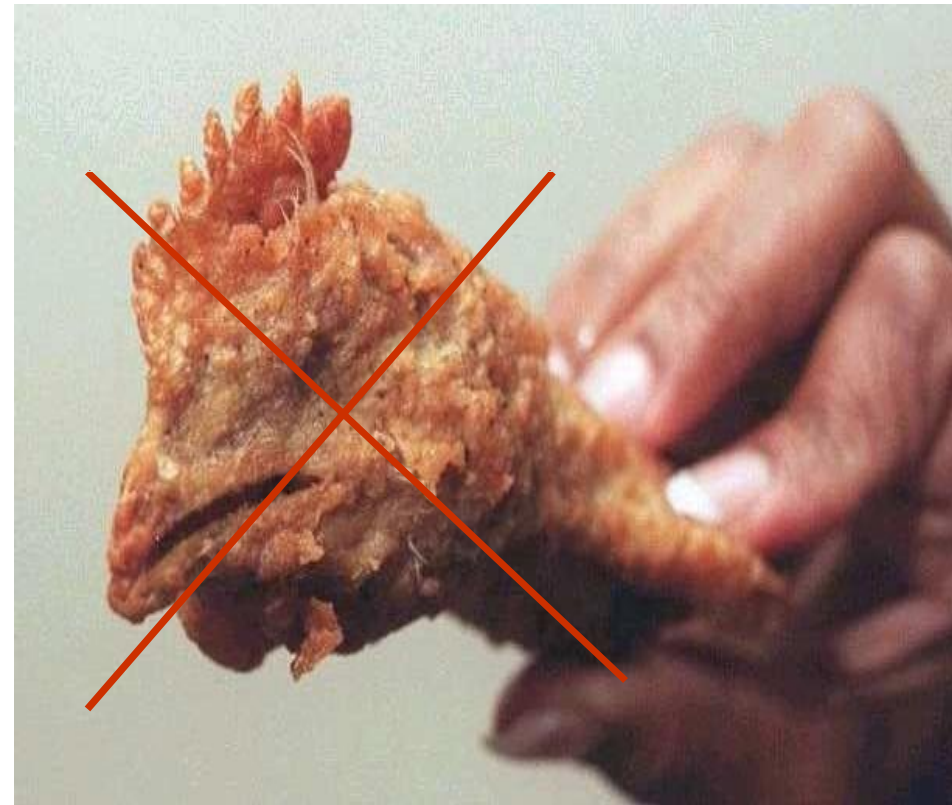


Strategies for Promoting Healthy
Eating, Exercise and Parent
Involvement

قَالَ رَسُولَ اللَّهِ ﷺ : مَا مَلَأَ آدَمِيَّ وَعَاءَ شَرًّا مِنْ بَطْنِهِ بِحَسْبِ ابْنِ آدَمَ
أَكْلَاتٍ يُقْمَنَ صُلْبَهُ فَإِنْ كَانَ لَا مَحَالَةَ فَتُلُتْ لِبَطْنِهِ وَتُلُتْ لِشَرَابِهِ وَتُلُتْ
لِنَفْسِهِ . رواه الترمذي وصححه الألباني

Most successful approach to weight maintenance or weight loss requires substantial lifestyle changes that include increased physical activity and altered eating habits

Prevention of obesity & its complications



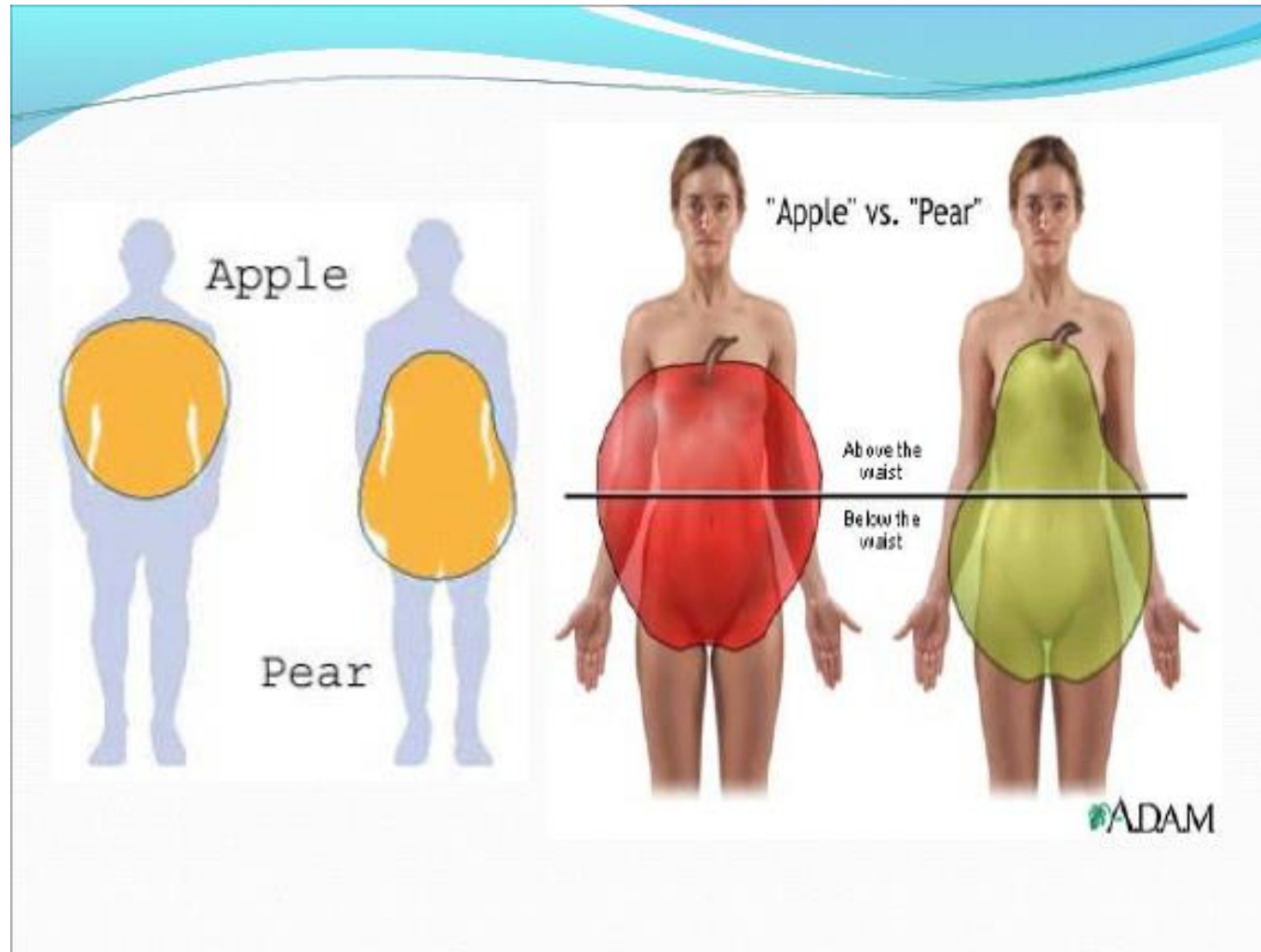
General Strategies

- Maternal health & weight reduction pre & throughout pregnancy.
- Encourage breast feeding.
- Increase consumption of fruits & vegetable
- Reduce screen time.
- Reduce soft drink consumption.
- Increase physical activity.

Obesity comorbidities

- Comorbidity management complicates the treatment of children with obesity.
- Insulin resistance / Type 2 DM
- HTN
- Dyslipidemia
- Sleep disorders
- Fatty liver disease
- Metabolic syndrome
- In female adolescents: PCOS
- Psychological / Behavioral changes

Android Vs Gynecoid Obesity



Epigenetic

- Is a term used to describe processes that result in heritable regulation of gene expression without a change in the base sequence of DNA sequence.
- Epigenetic is thought to play a large role in the precipitous rise in obesity over the past 30 years.
- Children are at increased risk for obesity if their parents have obesity: there is a 30% chance of obesity if one parent has obesity and a 90% chance if both parents have obesity.
- Obesity in childhood is associated with a maternal preconception BMI (body mass index) 30 kg/m^2 , excessive gestational weight gain, and gestational diabetes mellitus.
- Infants who are small for gestational age due to tobacco abuse or insufficient maternal weight gain are also at risk for obesity and metabolic disease in childhood.

Management of Obesity

- Successful treatment of obesity is challenging !!
- Treatment goals vary- depending on age of the child & the severity of complications.
 - Dietary management (healthy diet & microbiota)
 - Exercise.
 - Behavior modification.
 - Medications.
 - Surgical approaches.
- Treatment of Complications

- Most successful approach to weight maintenance or weight loss requires substantial lifestyle changes that include increased physical activity & altered eating habits
- Severely overweight children & adolescents with complications from obesity are best managed by a multidisciplinary team.
- Teams may include a physician, a psychologist, a dietitian, an exercise specialist , a nurse, and counselors.
- The treatment models used in most pediatric centers feature family based behavioral treatment, which is the only approach shown to have long-term efficacy.

- Managing a child with obesity is age dependent.
- In the first 6 months of life, exclusive breast feeding is the nutrition of choice.
- Complementary foods should ideally be delayed until 6 months of age.
- Increased BMI in childhood & adolescence is associated with early introduction of complementary foods.
- Infants with obesity should not be given any sugar sweetened beverages, nor any fast food or desserts.
- Infants already struggling to maintain their weight should have age appropriate amounts of formula, and should not be given juice in their bottles.
- Infants should not be watching TV or any screen of any kind for the first two years of life.

- Up to the age of 2 years, no screen time is recommended.
- Between the ages of 2 and 4, screen time should be kept to a minimum.
- Obesity is directly correlated with screen time in this age group.
- The family should adopt good **meal hygiene** to include meals at the table, no media while eating, no food rewards, no over controlling behaviors toward consumption of meals, and family based meals.
- Obesogenic medications may be a factor for the young child with obesity (aged 5–9 years).
 - The use of second generation antipsychotics should be minimized and asthma should be managed with controller medications instead of systemic steroids if clinically possible.

- Parents are strong role models for children and involvement of the family in the care of the child with obesity is highly recommended.
- Replacement of screen time with moderately vigorous physical activity is associated with a decrease in obesity.
- Children with obesity in the 5–9 age group should be consuming 3 meals per day plus 1–2 nutritious snacks.
- Food groups should include 3 servings of protein per day, 1–2 servings of dairy per day, and 4–5 servings of non-starchy vegetables per day.
- They should not be consuming any sugar sweetened beverages, nor any fast food.
- Total non-academic screen time should be kept to a minimum.

Modeling can not be underestimated!



Management of the Infant with Obesity: 0-24 Months

- NO screen time
- NO TV in bedroom
- Allow infant to feed themselves
- Do not force/finish foods when infant indicating refusal
- 12-18 hours of sleep



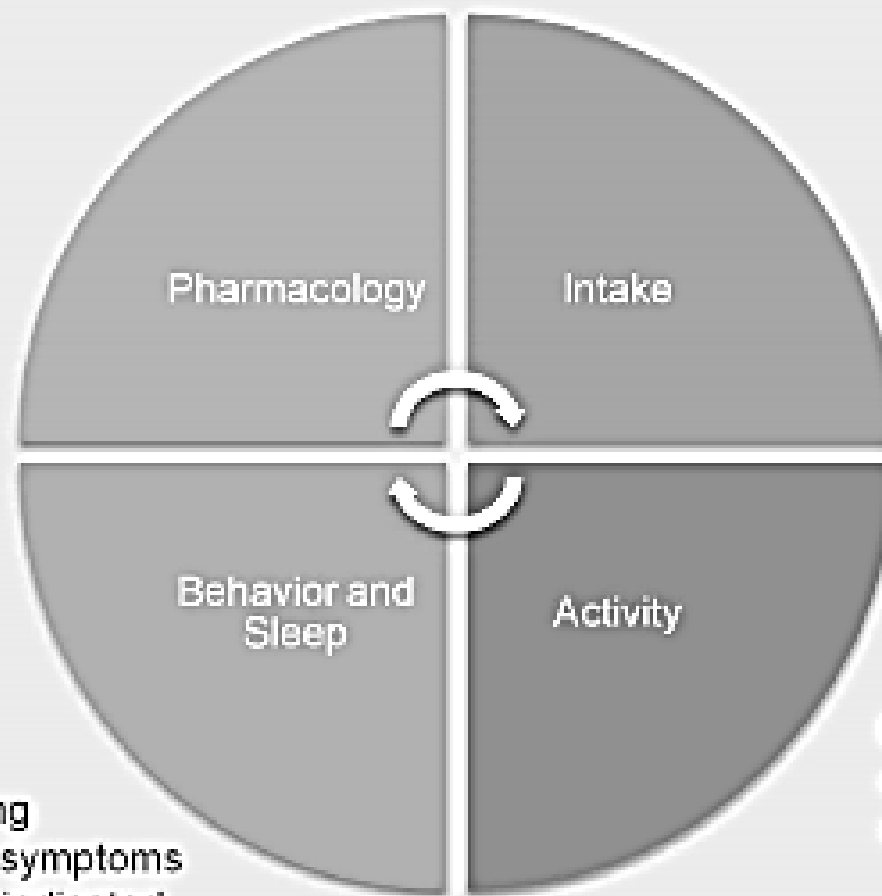
- Exclusive breastfeeding for 6-12 months
- Appropriate formula feeding ingestion for age
- Delay complementary foods until 6 months
- NO juice/sugar-sweetened beverages
- NO fast food
- NO desserts

- Keep active in playpen/floor
- Encourage direct interaction with parents as much as possible
- No media

Management of the Young Child with Obesity: 5-9 Years

- Minimize obesogenic medications especially second-generation antipsychotics (SGAPs)
- Treat asthma with controller meds to minimize systemic steroid use
- Consider ACE inhibitor for persistent hypertension

- Screen time < 1-2 hours
- Routine sleep pattern
- No TV in bedroom
- 11-14 hours of sleep
- All meals at the table
- Parents as role models
- Parents should not be over-controlling
- Sleep study if severe obesity and/or symptoms
- Tonsillectomy and adenoidectomy if indicated



- Three meals; 1-2 snacks
- 3 servings of protein/day
- 2-3 servings of dairy/day
- 1.5-2 servings of fruit/day
- 4-5 servings non-starchy vegetables
- Dessert only on special occasion
- NO sugar-sweetened beverages
- NO fast food
- Age-appropriate portion sizes
- Praise for trying new foods
- Consider LGI/reduced-CHO diet

Moderate to vigorous activity for 60 minutes or greater each day; can be organized or not

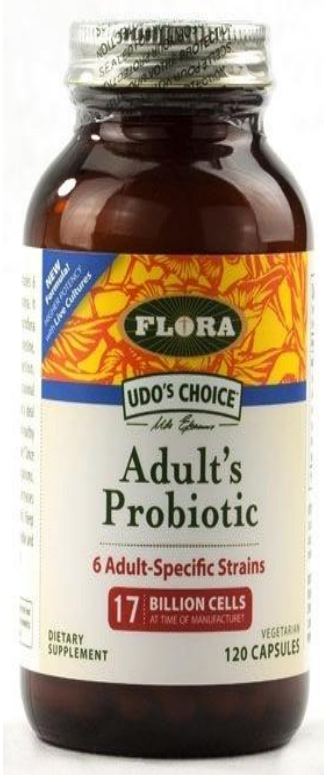
Exercise

- Decreasing sedentary activity is essential for achieving weight control.
- Increased activity not only increases calorie use but also appears to decrease appetite.
- Children younger than 2 years, avoiding television and computers
- Children 2–18 year of age should have <2 hour/day of “screen time” (television, video games, computer), and televisions should be removed from children's bedrooms.
- Better option to decrease inactivity
 - Less time on computer/ TV
 - Using stairs in place of elevators
 - Walking to perform daily errands
 - Playing outdoor games

Behavior Modification

- Psychologists screen families for underlying problems that led to child's overweight.
- Once problems are identified, psychologists and counselors can use cognitive behavioral and family therapy to address such issues.
- The treatment models used was family-based behavioral treatment, which is the only approach shown to have long-term efficacy.

Pre/Probiotics as for healthy intestinal microbiota

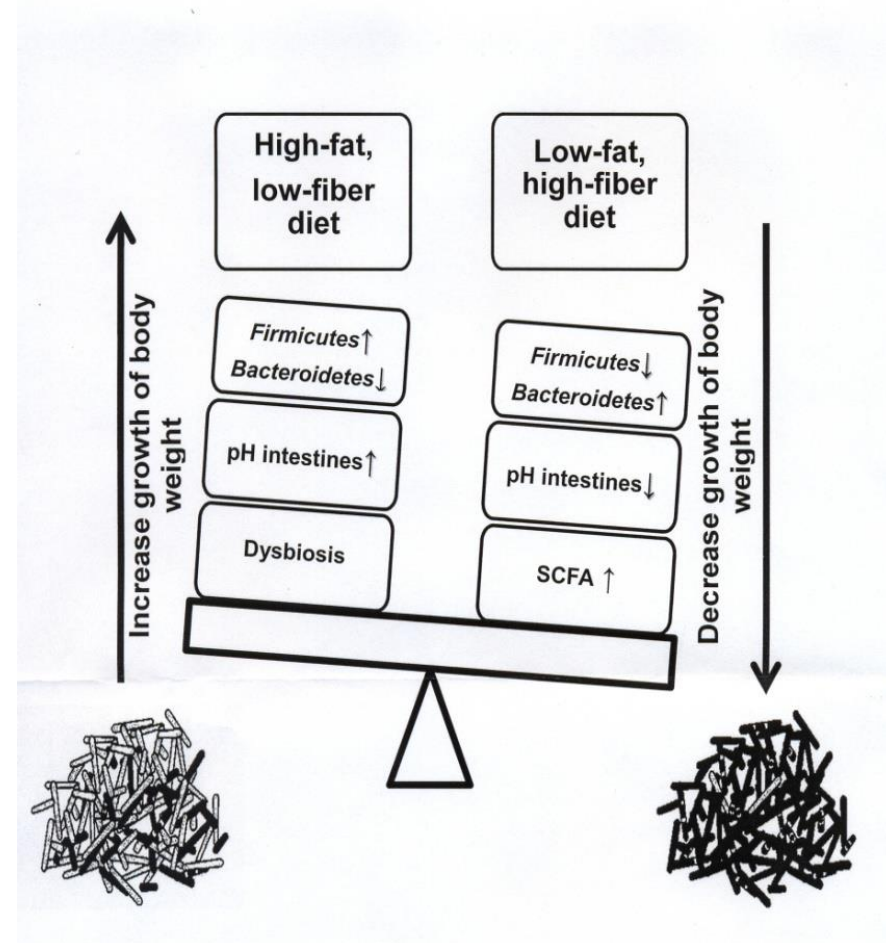




Gut Microbiota

A healthy gut is the sign of healthy life

High Fiber diet will increase proportion and function of gut Microbiota



Diet →
eg. Western diet

Dysbiosis
of
gut microbiota

host gene expression

energy harvest

chronic inflammation

Obesity

other factors:
Age
Lifestyle
Genetics
Antibiotic usage

other diseases:
IBD
Diabetes
Cancer
Autism

Anti-obesity Medications

- These medications should be used as adjuncts to healthy eating, good nutrition, increased physical activity, and behavior modifications.
- BMI ≥ 30 kg/m² or a BMI ≥ 27 kg/m² and at least 1 obesity-related comorbidity (e.g., hypertension, dyslipidemia, type 2 diabetes, and obstructive sleep apnea).
- The dose of each agent should be escalated based on efficacy and tolerability and should not exceed the maximum dose listed on the agent's prescribing information.
- The efficacy and safety of weight loss medications should be assessed monthly for the first 3 months and every 3 months thereafter.
- Treatment efficacy is defined as weight loss of $\geq 5\%$ at 3 months.

Pharmacology

Orlistat (Xenical)

- FDA-approved for children ≥ 12 years
- Weight loss is small
- Side effects preclude usage in most patients
- May cause oily stools

Metformin

- FDA-approved for children with T2DM ≥ 10 years
- Weight loss is small
- Useful for elevated serum insulin levels
- May prolong duration of time before onset of T2DM
- May cause gastrointestinal upset, especially in first few weeks

Topiramate

- Not FDA-approved for weight loss in children
- Has been used for seizure control in children for years
- May control cravings
- Can cause cleft palate in fetus
- May cause paresthesias of extremities, cognitive disruption (confusion, difficulty concentrating)

Phentermine

- FDA-approved for weight loss in children ≥ 16 years
- Has been used in adolescents
- Weight loss is small to moderate
- May cause anxiety, tremors, slightly increased blood pressure

Agent	Mechanism of Action	Notes
Diethylpropion	Norepinephrine-releasing agent	Approved for short-term use (3 months)
Liraglutide (Saxenda)	GLP-1 receptor agonist	Recommended for patients with cardiovascular disease
Lorcaserin (Belviq)	5HT _{2c} receptor agonist	
Natrexone/bupropion (Contrave)	Opioid antagonist/dopamine and norepinephrine reuptake inhibitor	
Orlistat, prescription (120 mg, Xenical) and over-the-counter (60 mg, Alli)	Pancreatic and gastric lipase inhibitor	Recommended for patients with cardiovascular disease
Phentermine	Norepinephrine-releasing agent	Approved for short-term use (3 months); Not recommended in patients with uncontrolled hypertension or heart disease
Phentermine/topiramate (Qsymia)	Norepinephrine-releasing agent/GABA receptor modulation agent	

GABA, γ -aminobutyric acid; GLP-1, glucagon-like peptide-1

Mode of Actions of Anti- obesity Agents

- Lowering appetite (all approved agents except orlistat)
- Blocking fat and calorie absorption (orlistat only)
- Amplifying adherence to behavior changes and allowing people to lose weight, these agents may improve physical functioning and allow for greater physical activity.
- **Avoid Off-Label Use of Medications for Weight Loss**
- **Other useful agents include:** exenatide, liraglutide, metformin, methylphenidate, thyroid hormones, topiramate, and zonisamide.

GLP-1 RAs

Human GLP-1 Backbone

QW

Dulaglutide

Dimeric DPP-4 resistant human GLP-1 genetically fused to the Fc domain of IgG4 ($t_{1/2}$ = 5 days)

Albiglutide

DPP-4 resistant human GLP-1 dimer genetically fused to human albumin ($t_{1/2}$ = 5 days)

QD

Liraglutide

Acetylated GLP-1 analog; Acetylation allows for association with albumin ($t_{1/2}$ = 13 hours)

Exendin-4 Backbone

BID

Exenatide BID

Synthetic exendin-4 peptide; 50% homologous to human GLP-1 and resistant to DPP-4 degradation ($t_{1/2}$ = 2.4 hours)

QW

Exenatide QW

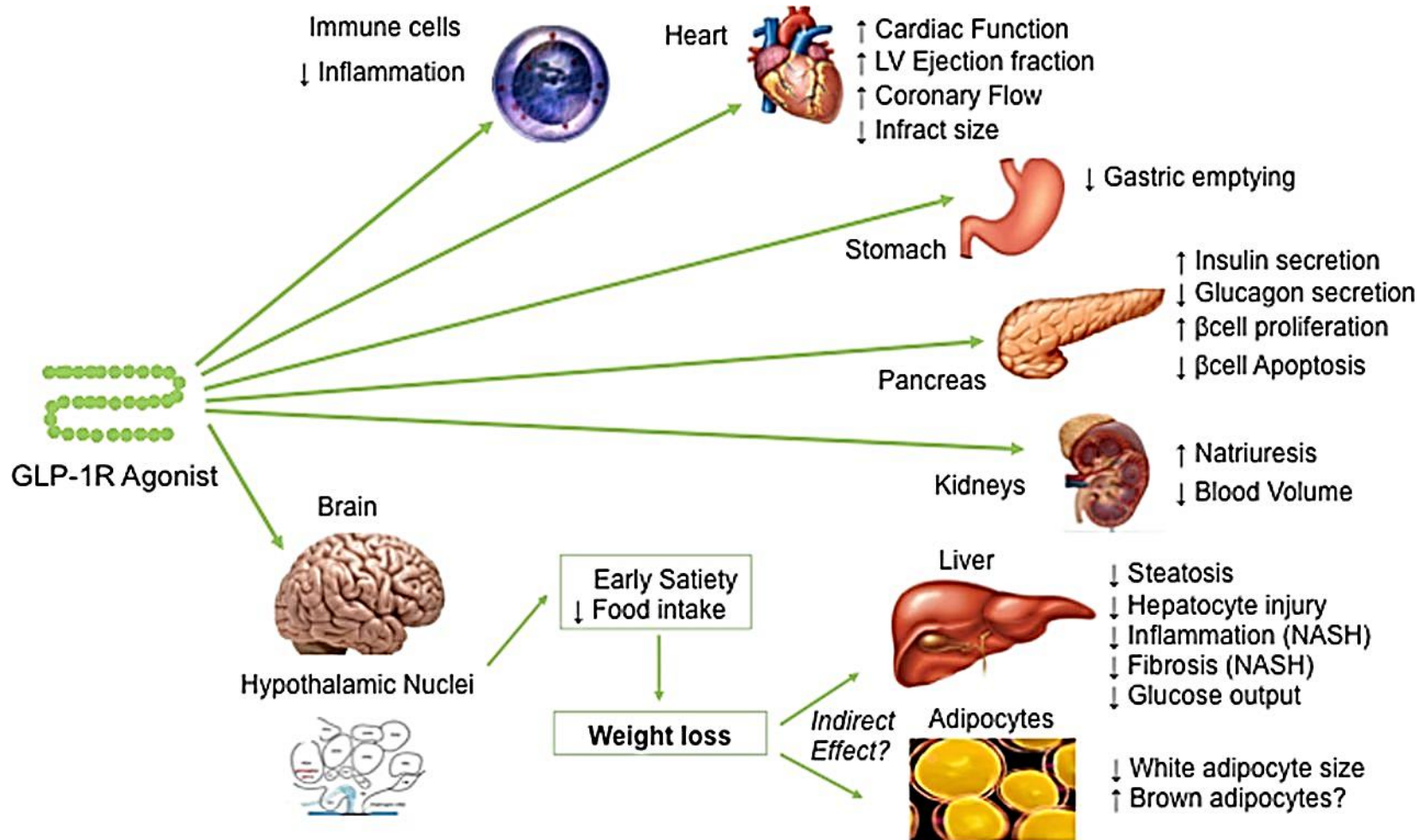
Exenatide encased in microspheres which slowly hydrolyze and extend release ($t_{1/2}$ = 2.4 hours)

QD

Lixisenatide

Synthetic exendin-4 peptide; C-terminal modification adding 6 lysine residues and removing 1 proline ($t_{1/2}$ = 3 hours)

Physiological effects of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in humans.



Gauri Dhir, and Kenneth Cusi *J Investig Med* 2018;66:7-10



New Drug Approved

- Trulicity
- Weekly Injection to Treat Type 2 Diabetes
- Indianapolis-Based Group Trying to Raise Profits

The Lilly logo is displayed in a red, cursive font on a white rectangular background.

NEW DETAILS

FDA APPROVES LILLY'S INJECTABLE DIABETES DRUG
TRULICITY IS A WEEKLY INJECTION FOR TYPE 2 DIABETES

rtv6 abc
THE INDY CHANNEL



This website is intended for U.S. Health Care Professionals

NEW
Saxenda[®]
liraglutide (rDNA origin) injection

Launching 2015

Trulicity GLP-1 agonist FDA approved for
clinical weight management



Metformin

- “**Glucophage**” is the first-line medication for the treatment of type 2 diabetes, particularly in people who are overweight.
- It is also used in the treatment of polycystic ovary syndrome.
- It is not associated with weight loss.
- It is taken by mouth.
- Metformin is generally well tolerated. Common side effects include diarrhea, nausea, and abdominal pain.
- It has a low risk of causing low blood sugar. High blood lactic acid level is a concern if the medication is prescribed inappropriately or in overly large doses.
- It should not be used in those with significant liver disease or kidney problems.

Surgical Approach

- Bariatric surgery is reserved as treatment for severe obesity in adolescents.
- The number of surgeries performed is increasing each year.
- Surgical options include gastric sleeve resection, gastric bypass & laparoscopic adjustable gastric banding under the treatment of an experienced surgical center.
- Current adolescent bariatric recommendations include:
 - BMI > 35 kg/m² with moderate to severe comorbidities
 - or BMI >40 kg/m²
 - skeletal & sexual maturity (generally age 14 for girls and 15 for boys).

Conclusions

- BMI should be measured periodically in all children .
- Child obesity is reaching alarming rates .
- Obesity is a multifactorial disease.
- Genetic and endocrine causes represent only 5% of all etiologies .
- Social and behavioral etiologies are the main culprit.
- Educating parents is an essential responsibility of pediatricians .
- Prevention is better than treatment الوقاية خير من العلاج

Conclusions

- Obesity is a chronic disease which when originating in childhood can lead to medical, psychological complications, in addition to premature comorbidity and mortality.
- A slowing of weight gain or lack of continued acceleration of weight gain can delay the onset of T2DM and early cardiovascular disease.
- In fact, addressing comorbid conditions such as obstructive sleep apnea, behavioral disorders, polycystic ovarian syndrome may be a necessary precursor to successful weight management.
- Clearly more needs to be done in our attempt to stop and eventually reverse this epidemic.

THANKS

