Random Diagnoses Your Patients Want You To Know

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Conflicts of Interest

- Speakers' Bureau for Rhythm Pharmaceuticals

Objectives

- Review pathophysiology & treatment of lipedema
- Review pathophysiology of genetic obesity
- Review pathophysiology & treatment of lp(a) elevation
- Summarize why these diagnoses are important for patients

Lipedema

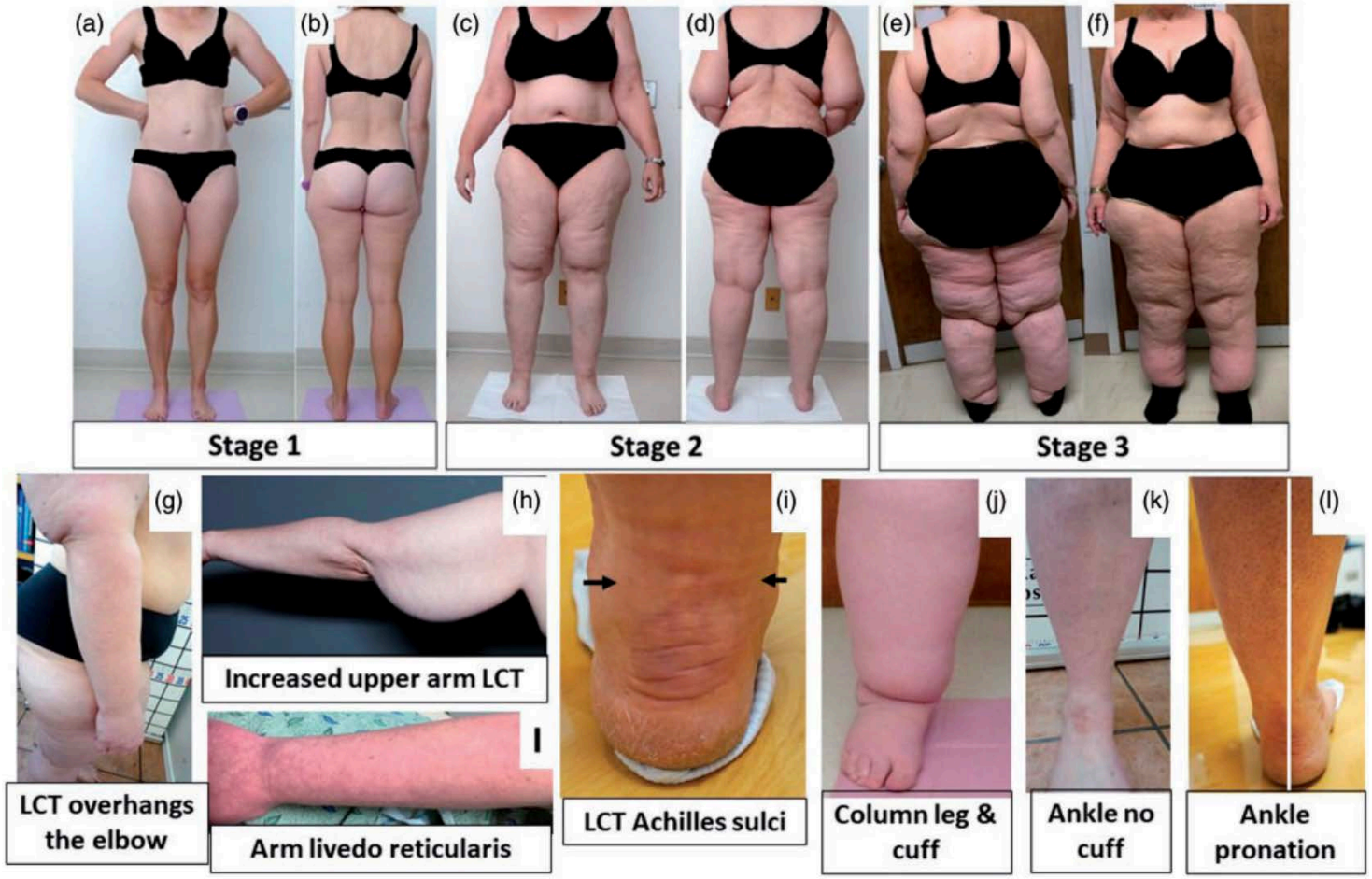


Figure 1. Herbst et al. 2021

Lipedema: Relevant Terminology

- Edema: By definition, “[edema] is an accumulation of fluid that manifests the classic pitting appearance of the soft tissues on clinical examination” (Bertsch, Erbacher, 2020).
- Lipohypertrophy: “A painless disproportionate increase in adipose tissue” (Concensus Document, 2020). “A condition in women that is very similar to lipedema but without edema or pain” (Herbst et all, 2021)
- Lipedema: “A chronic condition characteri[z]ed by a disproportionate increase in adipose tissue and pain in the legs and, sometimes, the arms of women.” (Concensus Document, 2020). It is “a disease of loose connective tissue (LCT) on the lower abdomen, hips, buttocks, and limbs [...] sparing the trunk, hands, and feet” (Standard 2021).
- Lipolymphedema: stage IV lipedema believed to be a pre-lymphedema condition (Herbst, 2020)

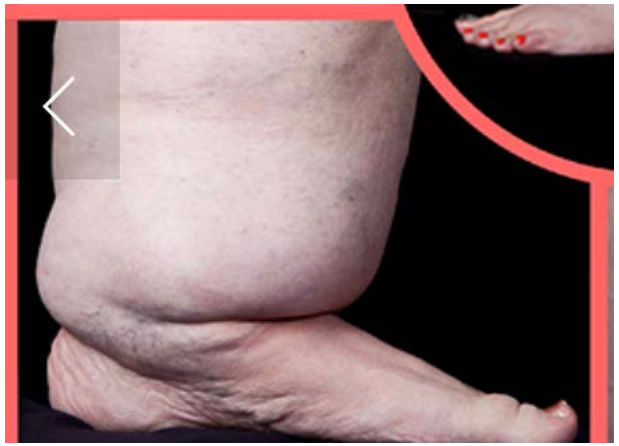
Lipedema: Brief History

- Allen and Hines first described it in 1940 at Mayo Clinic and created the name lipedema based on the assumption it was a disorder of edema when this is not a disorder of edema nor lymphatic channel insufficiency. (Allen, 1940) (Wold, 1951)
- There were only a few individual case reports on lipedema or painful adipose tissue in the 1960s and 70s. (Muller, 1973) (Greer, 1974)
- Lipedema began to gain traction again after “The fat leg in the healthy woman’ in the journal Gynäkologie. (Schmitz, 1980)

Lipedema Clinical Picture

- Difficult losing weight in particular parts of the body (hips, thighs, calves, buttock, underarms, below umbilicus of abdomen)
- Easy bruising/ vascular fragility
- Cool tissue on appendages that differ significantly from other parts of the same appendage
- Nodules or lipomatous tissue under the skin that may or may not be painful
- Hyperflexibility/hypermobility
- Cuffing at the wrist, ankle, elbow, or knee

- Commonly starts during puberty, after childbirth or menopause
- Loss of tissue elasticity



Figures 2 & 3. Lipedema Foundation. 2022

Lipedema Staging

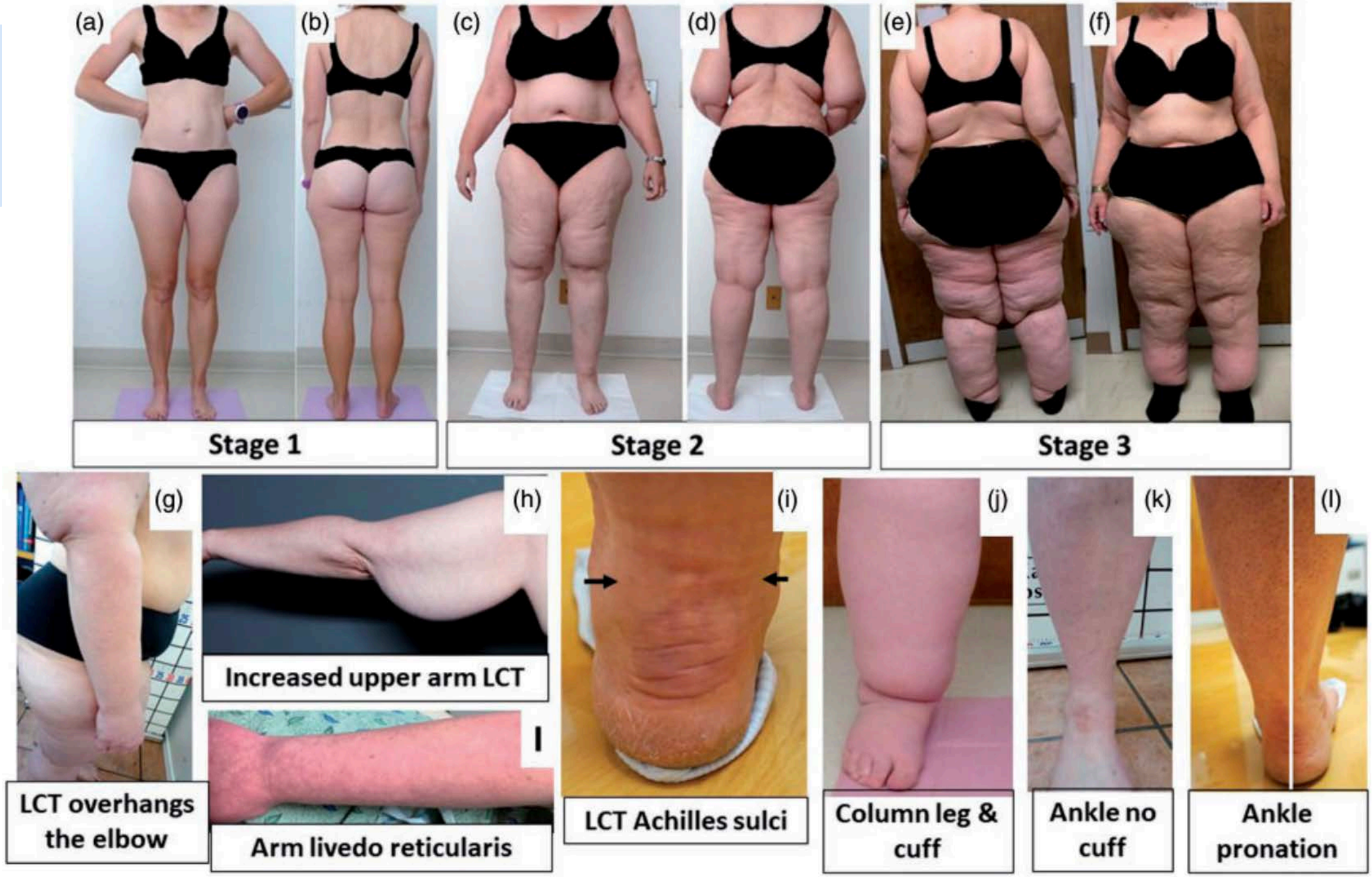
Stages	Skin	Subcutaneous Fat	Lymph-edema
1	Subdermal pebbles	Enlarged hypodermal SAT; wrists/ankles may begin to cuff	-
2	**Indentations/dimpling**	**Larger mounds** with non-encapsulated masses; **Full achilles sulci; upper arms began to hang; wrists/ankles more markedly cuff**	-
3	**Extrusions/overhanging lobules, multiple subdermal nodules**	Gross deformations on thighs and around knees	-
4 (lipo-lymphedema)	extrusions	Gross deformations on thighs and around knees	**+**

Table 1. (Adapted from Herbst et al., 2021)

Lipedema Type

Types	Location
1	Under umbilicus and on hips and buttocks
2	Umbilicus to knees
3	Umbilicus to ankles
4	arms
5	Lower legs

Table 2. (Adapted from Herbst et al. 2021)


(a)
(b)
(c)
(d)
(e)
(f)
Stage 1
Stage 2
Stage 3
(g)
(h)
(i)
(j)
(k)
(l)
LCT overhangs the elbow
Increased upper arm LCT
Arm livedo reticularis
LCT Achilles sulci
Column leg & cuff
Ankle no cuff
Ankle pronation

Lipedema Staging

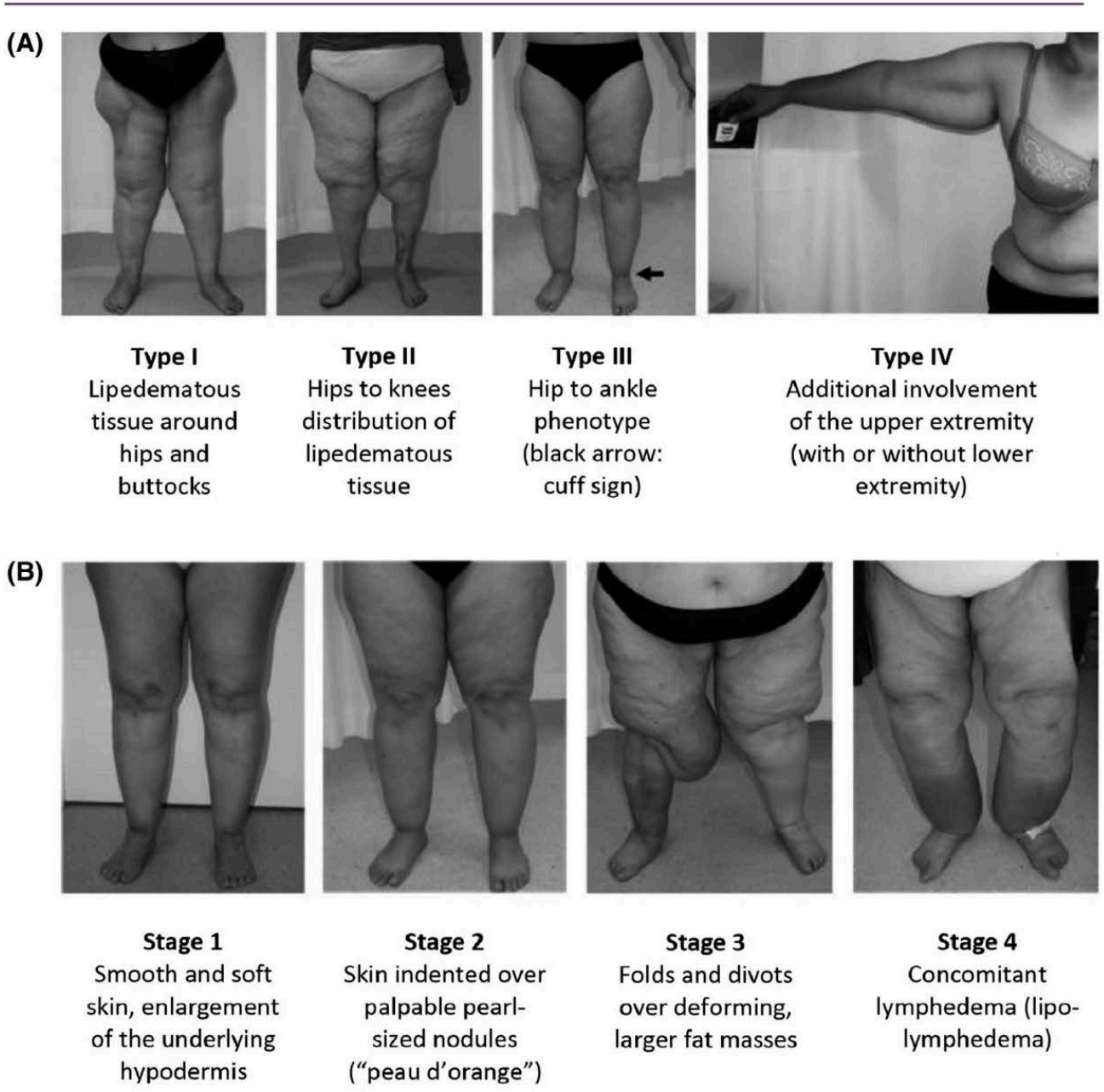


Figure 1 **(A)** Types and **(B)** stages of lipedema.

Figure 4. Buso et al., 2019

Lipedema: Epidemiology

- A minimum value of 1:72,000 (Child et al, 2010) on the low side to as many as 18.8% (Forner-Cordero et al, 2012); however, most cite and lend to numbers close to 11% (Foldi et al). 6%–8% in women in Germany and 15%–19% in vascular clinics (Herbst et al, 2021)
- Lipedema affects mostly women. Most report it starting in puberty, but others report pregnancy, OCP therapy, or menopause. (Child et al, 2010)
- Men can have lipedema, but it is less common. Male patients “tend to have concomitant conditions associated with higher estrogen and lower relative testosterone levels, such as male hypogonadism and liver disease” (Szel, 2014; Bano, 2010; Chen, 2004)
- Patients with lipedema also having obesity and overweight range from 91.3% to 97% and 80-85% had obesity alone (Bertsch, 2015; Bosman, 2011; Child, 2010; Herbst, 2015; Dudeck, 2018)
- Positive family history in 16-64%. Suspected polygenic vs AD with incomplete penetrance (Buso, 2019).

Lipedema: Measurement Tools

- hrUS (with a 18.6- MH transducer + Moisture Meter) has been used to see that the edema is scant and same between lipedema and lipohypertrophy patients
- CT scan
- Lymphoscintigraphy
- Indirect lymphography
- MR lymphography of the lower extremities has not demonstrated signs of edema in pure lipedema patients (15).
- Dynamic lymphoscintigraphy:
- Fluorescence microlymphography

Consensus Document, 2020

Fat Accumulation Disorders

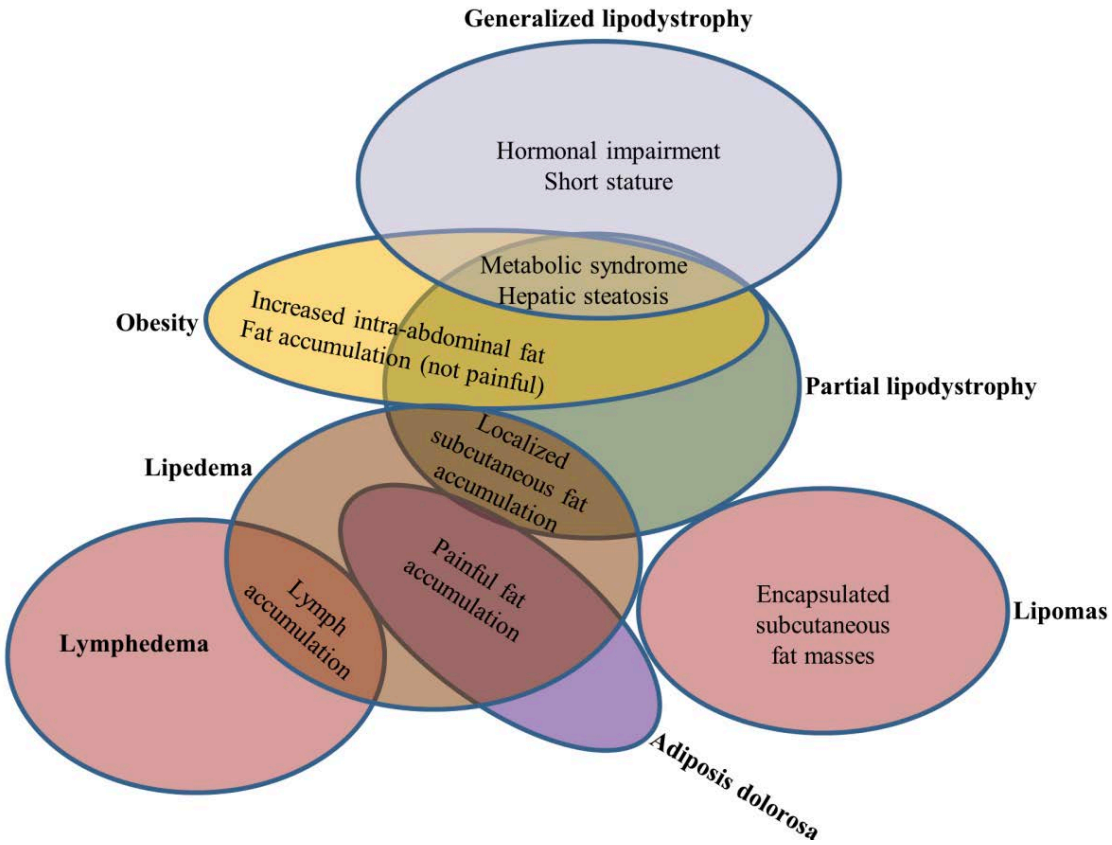


Figure 5. Paolacci, 2019

Lipedema Pathophysiology

Lipedema patients have excess sodium rich fluid (Crescenzi, 2018)–>

Increased fluid increases LCT compliance which allows more fluid to collect and stimulates proteoglycan production->

Sodium rich fluid exits adipose into extracellular tissue ->

Glycosaminoglycans increase when extracellular matrix water and/or salt increases->

Fluid is bound to glycosaminoglycans and proteoglycan due to proteins' strong negative charge->

Excess fluid limits cell access to oxygen resulting in hypoxia, inflammation and fibrosis

Herbst et al. 2021

Lipedema Pathyophysiology

- Expanding adipose tissue → low grade hypoxia→ low grade inflammation → pro-inflammatory adipokines → further inflammation and release of hypoxia-inducible factors (HIF1a) (Peled, 2016; Pou, 2007; Stulnig; 2009; Halberg, 2009; Fujisaka, 2013; Rutkowski, 2009; Mancuso, 2016)
- Histology: isolated foci of fat necrosis & increased numbers of antiCD68+ macrophages in the interstitial tissue (Kayserling, 2001). There are greater numbers of M2 macrophages vs M1 macrophages (Herbst, 2021)
- Red blood cells & malondialdehyde as biomarkers of oxidative stress found to be higher than those with lipedema than in healthy patients (Brenke, 2001)
- Over 28 genes have been identified in association with lipedema (Paolacci, 2019)
- Genes involved in decreased breakdown of Progesterone or decreased ER-alpha in comparison to ER-beta

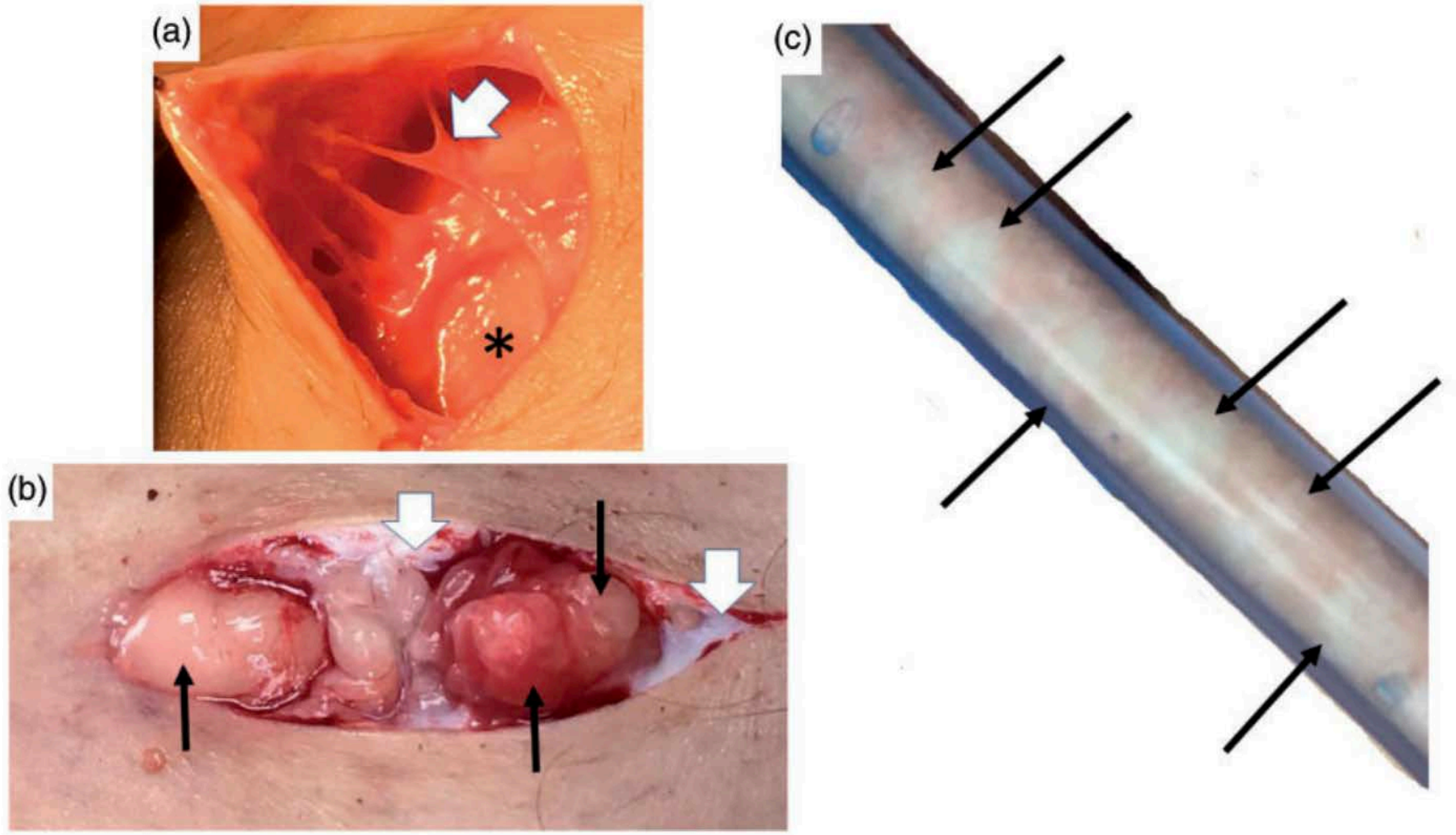
TABLE 1 Diagnostic criteria of lipedema

Medical history (A) (criteria of Wold et al. (17))		
A		**1** Disproportionate body fat distribution
		2 No or limited influence of weight loss on fat distribution
		3 Limb pain and bruising
		4 Increased sensitivity to touch or limb fatigue
		5 Nonpitting edema
		6 No reduction of pain or discomfort with limb lift
Physical examination (B, C, D, E)		
B	**Proximal part of the lower limb**	
		1 Disproportionate fat distribution
		2 Circumferentially thickened cutaneous fat
C	**Distal part of the lower limb**	
		1 Proximal thickening of subcutaneous fat
		2 Distal thickening of subcutaneous fat, accompanied by slender instep (cuff sign)
D	**Proximal part of the arm**	
		1 Significantly thickened subcutaneous fat in comparison with vicinity
		2 Sudden stop at elbow
E	**Distal part of the arm**	
		Thickened subcutaneous fat, accompanied by slender back of hand (cuff sign)
Extra criteria		
F		**1** Pain when applying bimanual palpation
		2 Distal fat tissue tendrils of the knee (popliteus)

Modified from Halk and Damstra (74).
Diagnosis is highly probable when present: A (1 to 6) + (B [1 + 2] or C [1 + 2] or D [1 + 2] or E).
In the absence of at most two of these criteria (A to E), the presence of the extra criteria F(1) or F(2) also support the diagnosis.

Table 3. Buso et al, 2019

Fibrotic Scar Tissue



Figures 6. Herbst et al. 2021

Lipedema & Concomittent Lymphedema

- Lymphography and lymphoscintigraphy demonstrate that lymph transport from the subepidermal compartment functions in lipedema, but does not in lymphedema (Harwood, 1996; Bautigam, 1998; Amann-Vesti, 2002)
- Bilancini et al found slowed lymph flow in patients with lipedema (Bilancini, 1995) and Amann-Vesti et al found microaneurysms of the lymph capillaries (Amann-Vesti, 2001).
- It's difficult to know if these physiologic changes were due to obesity or lipedema itself.
- Obesity is likely main factor contributing to edema and not lipedema itself. Lymphatic vessels are surrounded by subcutaneous fatty tissue contributing to mechanical compression→ pro-inflammatory adipokines like TNF-alpha, HIF1a increase from SAT and adiponectin (protective) decreases→ resultant damage to the lymphatic vessels (Bertsch, 2018)

Lipedema: Treatment

Figure 7. Consensus Document, 2020

Lipedema: Treatment

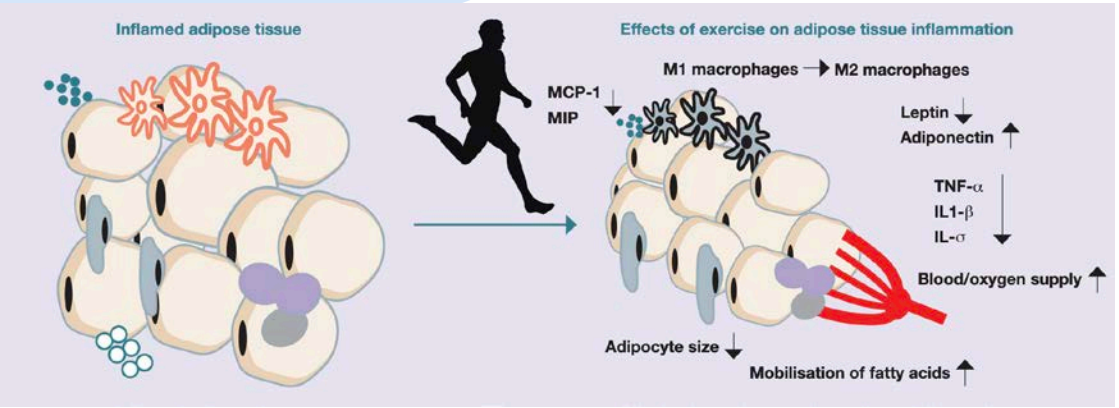
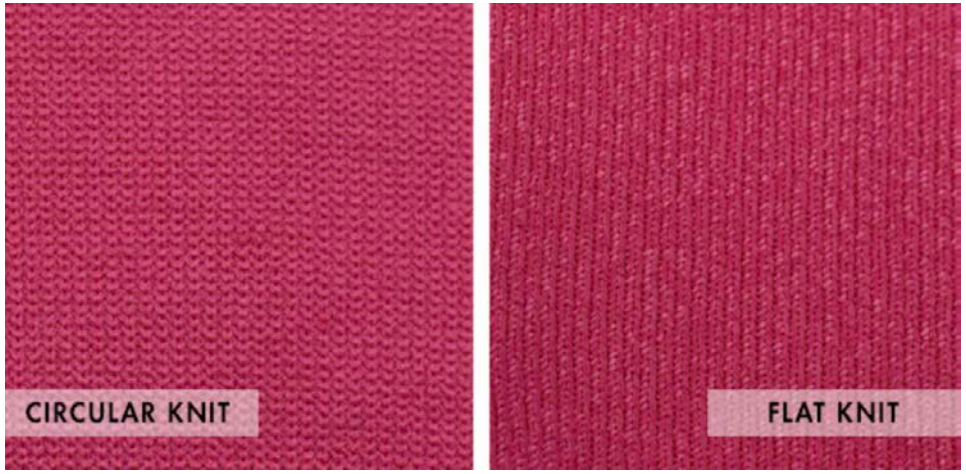


Figure 8. Consensus Document, 2020

Figure 10. Pexels.com

Figure 9. Lymphedivas.com



- flat-knit compression hosiery every day

10-20 mmHg for prevention; 20-30 for stage 2

And 30-40 mmHg for stage 3

- regular exercise 2–3 times every week
- Manual Lymphatic Drainage (MLD): The committee for the International Joint Census statement states did not advise MLD despite knowing some patients recognize benefit because the committee felt there was a lack of proven efficacy and there may be confounding with touch/attention/stress relief (Consensus Statement, 2020)

Lipedema & Surgery

Figure 11. Consensus Document, 2020

University of Freiburg in conjunction with the Földi Clinic found a 33.7% adjusted leg volume reduction in lipoedema patients following bariatric surgery. (Fink, 2020)

In two large studies, 70-77% of the patients still required complex decongestion after liposuction (Schmeller, 2010; Murad, 2016). Neither had sham groups.

Authors posit weight of suctioned adipose tissue in total body fat and leg fat will increase within a year (Hernandez 2011).

Lipedema: Treatment

Liposuction

- 1. The symptoms persist despite at least 12 months of conservative treatment mentioned above
- 2. The patient has considerable functional disabilities (e.g. restricted mobility)
- 3. The patient's weight has been stable for at least 12 months. This reduces the risk of the effects of liposuction being cancelled out by postoperative weight gain.
- 4. A preoperative psychological assessment is available, to rule out any eating disorders or relevant mental health issues that might hamper sustained treatment success.
- 5. BMI no more than 35 kg/m2.

Consensus Document, 2020

Obesity

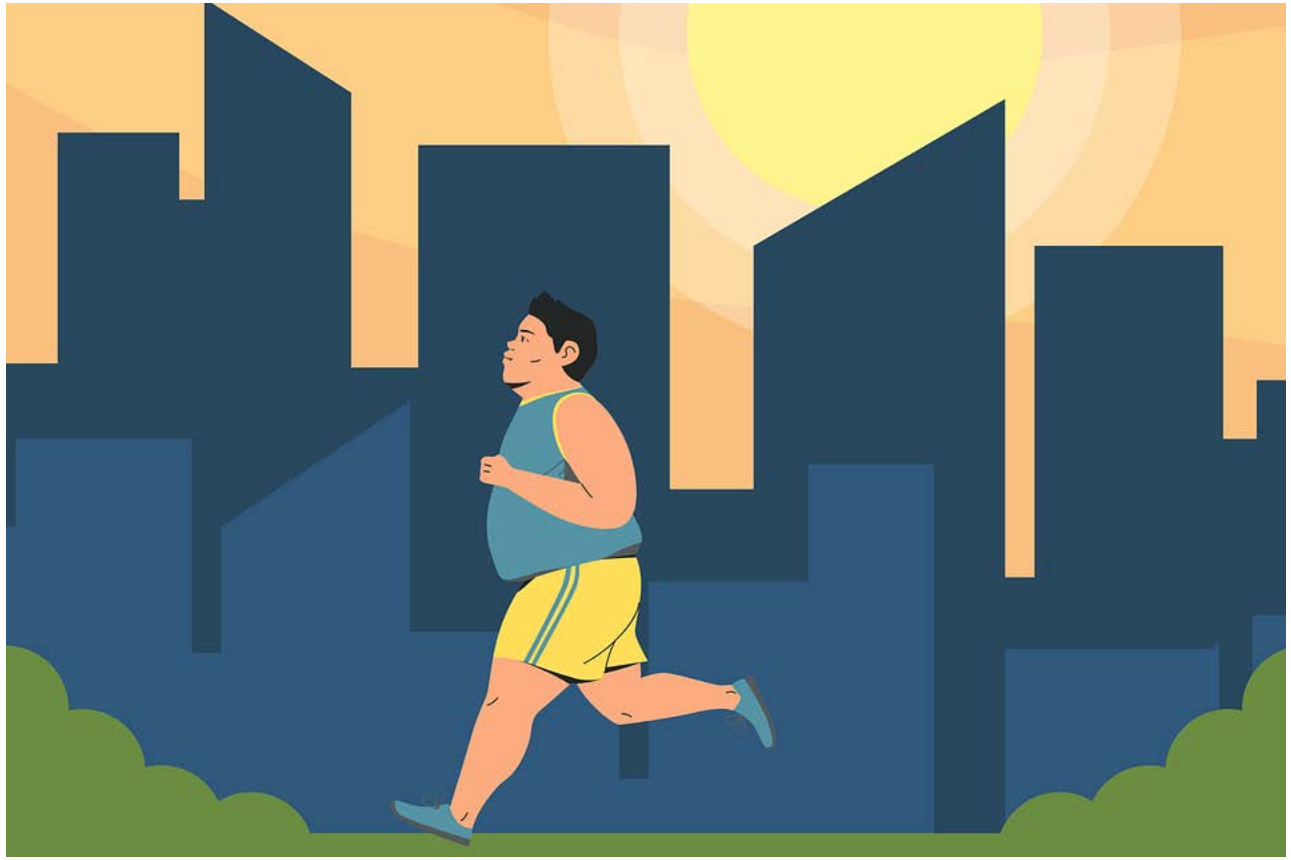
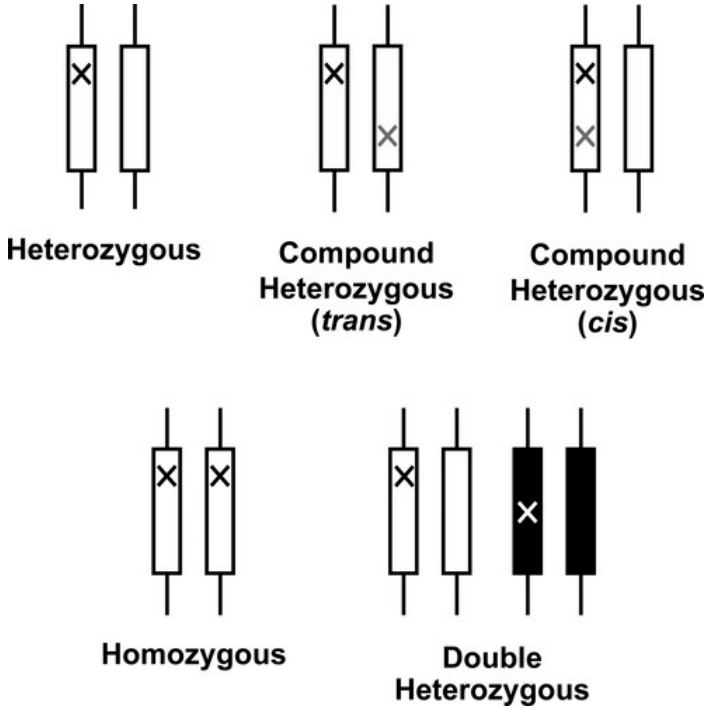


Figure 12. pixabay.com

Rare Genetic Disorders of Obesity (RGDO)



Common
Polygenic risk

Rare
Heterozygous (AD), compound heterozygous, homozygous mutations

Figure 13.
Kelly 2009

- ADCY3, AFF4, ALMS1, ARL6, BBIP1, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, BDNF, CEP290, CFAP418, CPE, CREBBP, CUL4B, DNMT3A, DYRK1B, EP300, GNAS, HTR2C, IFT172, IFT27, IFT74, INPP5E, ISL1, KIDINS220, KSR2, LEP, LEPR, LZTFL1, MAGEL2, MC3R, **MC4R**, MECP2, MKKS, MKS1, MRAP2, NCOA1, NR0B2, NRP1, NRP2, NTRK2, PCNT, PCSK1, PHF6, PHIP, PLXNA1, PLXNA2, PLXNA3, PLXNA4, POMC, PPARG, PROK2, RAB23, RAI1, RPGRIP1L, RPS6KA3, SDCCAG8, SEMA3A, SEMA3B, SEMA3C, SEMA3D, SEMA3E, SEMA3F, SEMA3G, SH2B1, SIM1, TBX3, TRIM32, TRPC5, TTC8, TUB, UCP3, VPS13B, WDPCP

Red: Treatable
Green: In development
Black: Being studied

Heymsfield, 2018

Obesity Epidemiology

- 2016: ~2 billion adults (39% of the world's adult population) had overweight (Loos, 2022).
- 2016: 671 million (12% of the world's adult population) had obesity. These rates have tripled from 1975 (Loos, 2022).
- If trends continue, it is expected that 1 billion adults (nearly 20% of the world population) will have obesity by 2025 (Loos, 2022).
- The US obesity prevalence was 41.9% in 2017 – March 2020 (CDC 2022)

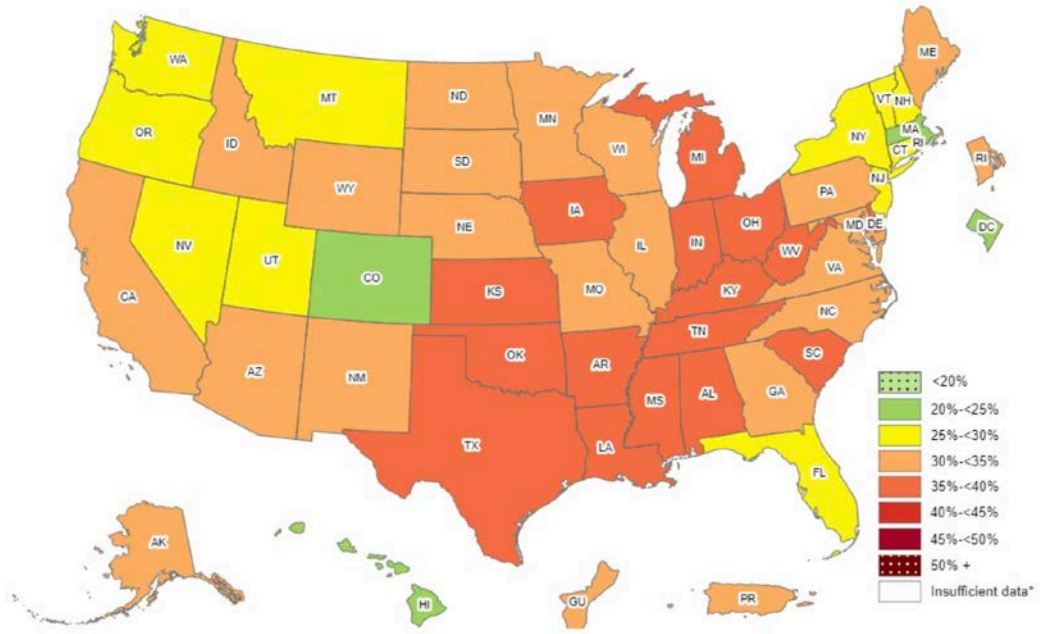


Figure 14. CDC, 2022

Genetic Obesity: RGDO Prevalence

Rare Genetic Disorders of Obesity Are Likely Underdiagnosed

True prevalence of rare genetic disorders of obesity is unknown because genetic testing is rarely done in individuals with obesity[1,2]

Gene or disorder	Estimated prevalence in the United States[a,b]
POMC deficiency obesity[3]	~100 to 500 individuals
LEPR deficiency obesity[3]	~500 to 2,000 individuals
Bardet-Biedl syndrome[3]	~1,500 to 2,500 individuals
Alström syndrome[3]	~500 to 1,000 individuals[c]
POMC or LEPR heterozygous deficiency obesity[3]	>20,000 individuals
SRC1 deficiency obesity[3]	>23,000 individuals
SH2B1 deficiency obesity[3]	>24,000 individuals
MC4R deficiency obesity[3]	~10,000 individuals[d]
Smith-Magenis syndrome[3]	~2,400 individuals
Prader-Willi syndrome[4]	>7,000 individuals

[a]Numbers reflect individuals appearing in detailed case histories from published literature or conference proceedings and do not include those appearing in reports such as genomic analyses or population screening studies. Analysis performed in June 2019.[3] [b]A list of LOF variants in *LEPR*, *POMC*, and *PCSK1* was compiled from published literature and supplemented with computationally predicted deleterious missense variants. The frequency of carriers, homozygotes, and compound heterozygotes for each gene was calculated using data from gnomAD sequencing data and the number of individuals with LOF variants of interest was estimated using Hardy-Weinberg proportions. Prevalence was estimated using a US population size of 300 million.[2] [c]Estimated prevalence worldwide. [d]Estimated prevalence with addressable variants of *MC4R*.

Table 4, Heymsfield, 2018

Obesity: Contributors to Weight

- Antibiotic Exposure
- Emotional state/Stress/Mental Health
- Endocrine disrupters
- Energy Density
- Epigenetics
- Exercise
- Food accessibility
- **Genetics**
- Habits
- Hobbies
- Improving Technology
- Leisure time/play
- Media
- Medical issues/Medication
- Physical Activity
- Sleep Duration
- Sleep Quality
- Social pressures
- Socioeconomic status
- Work activities

Genetic Obesity: Why Screen

- Obesity in young adulthood is associated with a 64% higher risk of mortality later in life and an 89% higher risk of cardiovascular disease related death (Hirko, 2015; Reilly, 2011)
- Obesity is a disease associated with multiple other comorbidities, not limited to: T2DM, OSA, CA, MDD/Anxiety, PCOS, OA, Sx complications, and NAFLD (Sources 69-76)
- Families and patients carry such incredible shame and stigma from their weight

Obesity: Diagnosis in Peds/Adults

ENDOCRINE SOCIETY

Age ≥2 years: CDC-normative BMI percentiles used[1]

Overweight: BMI ≥85th percentile

Obese: BMI ≥95th percentile

Extremely obese: BMI ≥120% of the 95th percentile or ≥35 kg/m^2

Obesity Medicine Association

CLINICAL LEADERS IN OBESITY MEDICINE®

Age 0 to <2 years: weight for length or BMI can be used[2,3]

Age ≥2 years: BMI used[2]

Overweight: BMI ≥85th percentile

Obese: BMI ≥95th percentile

- Class I: >95th percentile
- Class II: >120% of the 95th percentile or BMI >35 kg/m^2
- Class III: >140% of the 95th percentile or BMI >40 kg/m^2

International Obesity TaskForce

Age 2 to 18 years: BMI used[3]

Severe obesity:

- Age 2 years: BMI >21.2 kg/m^2
- Age 5 years: BMI >20.8 kg/m^2
- Age 18 years: BMI >35 kg/m^2

Obesity: Hyperphagia

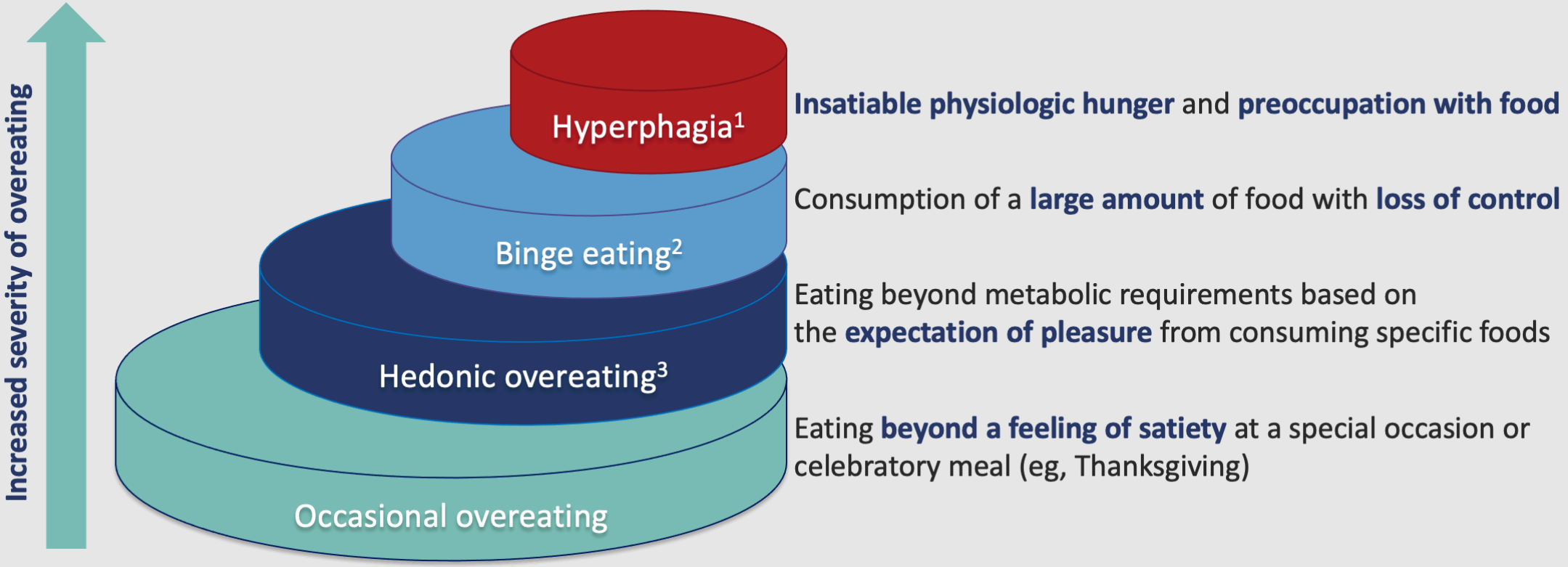


Figure 15. Heymsfield, 2014

Obesity: Satiation and Satiety

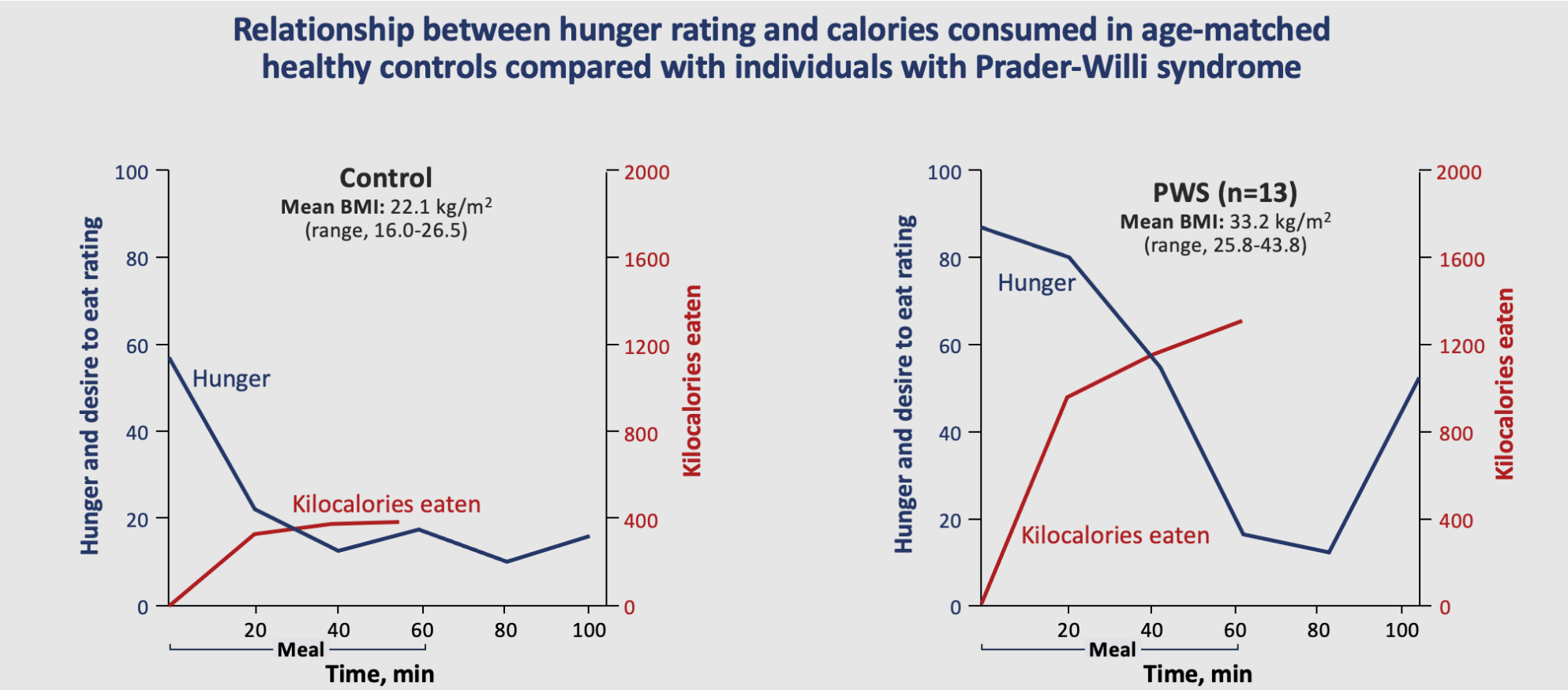


Figure 16. Holland, 1995

Genetic Obesity: Clinical Symptoms

Disorder	Early-onset obesity	Hyperphagia (insatiable hunger)	Growth	Endocrine abnormalities	Other
LEP deficiency[1,2]	✓	✓	Normal linear growth with reduced adult height	Hypogonadotropic hypogonadism, hypothyroidism	Alterations to immune function Responsive to leptin therapy
LEPR deficiency[1,2]	✓	✓	Normal linear growth with reduced adult height	Hypogonadotropic hypogonadism, hypothyroidism	Alterations to immune function Not responsive to leptin therapy
POMC deficiency[3-5]	✓	✓	Accelerated childhood growth[6]	Adrenocorticotropic hormone deficiency, mild hypothyroidism	Red hair, light skin
PCSK1 deficiency[4,7,8]	✓	✓[9,a]	Failure to thrive in early infancy	Hypoglycemia, hypothyroidism, adrenocorticotropic hormone deficiency	Intestinal malabsorption, diarrhea
MC4R deficiency[1,4,10,b]	✓	✓	Increased lean body mass, accelerated linear growth	Hyperinsulinemia	May have lower blood pressure
Alström syndrome[11,12]	✓	✓	Short stature	Type 2 diabetes mellitus, insulin resistance, hypogonadism, hyperandrogenism in females, hypothyroidism	Visual impairment, hearing loss, cardiomyopathy, hepatic dysfunction, renal failure

Table 5. Sources 78-87

Genetic Obesity: Clinical Symptoms

Disorder	Early-onset obesity	Hyperphagia (insatiable hunger)	Growth	Endocrine abnormalities	Other
Bardet-Biedl syndrome[1]	✓	✓	Wide range in height; does not differ significantly from population mean[2]	Hypogonadism	Visual impairment, cognitive disabilities, polydactyly, renal dysfunction
Smith-Magenis syndrome[3,4]	✓ Often by adolescence	✓ Often by adolescence	Short stature	Disrupted melatonin signaling	Self-injurious behaviors, sleep disturbances, craniofacial abnormalities, intellectual disability
SRC1 deficiency[5]	✓	Under investigation[6]	n/a	Impaired leptin-induced *POMC* expression	n/a
SH2B1 deficiency[7,8]	✓	✓	Reduced adult height	Hyperinsulinemia	Delayed speech and language development, aggressive behavior
Prader-Willi syndrome[1,9]	✓ Often by school age	✓ Neonatal period: decreased sucking, failure to thrive; age 4-8 y: excess hunger with major food impulsiveness	Short stature	Growth hormone deficiency, hypogonadism	Severe neonatal hypotonia, body composition abnormalities, intellectual deficiency, behavioral difficulties, dysmorphia
16p11.2 microdeletion syndrome[1,10]	✓ Often by adolescence	✓	Slightly below average or average height	n/a	Developmental delay, intellectual disability, autism spectrum disorders, impaired communication and socialization skills
Sim1 deficiency[1,11]	✓	✓	Short stature	Hypopituitarism	Developmental delay, neonatal hypotonia, facial dysmorphisms

Table 6. Sources 78-87

Genetic Obesity: Melanocortin 4 Receptor Pathway

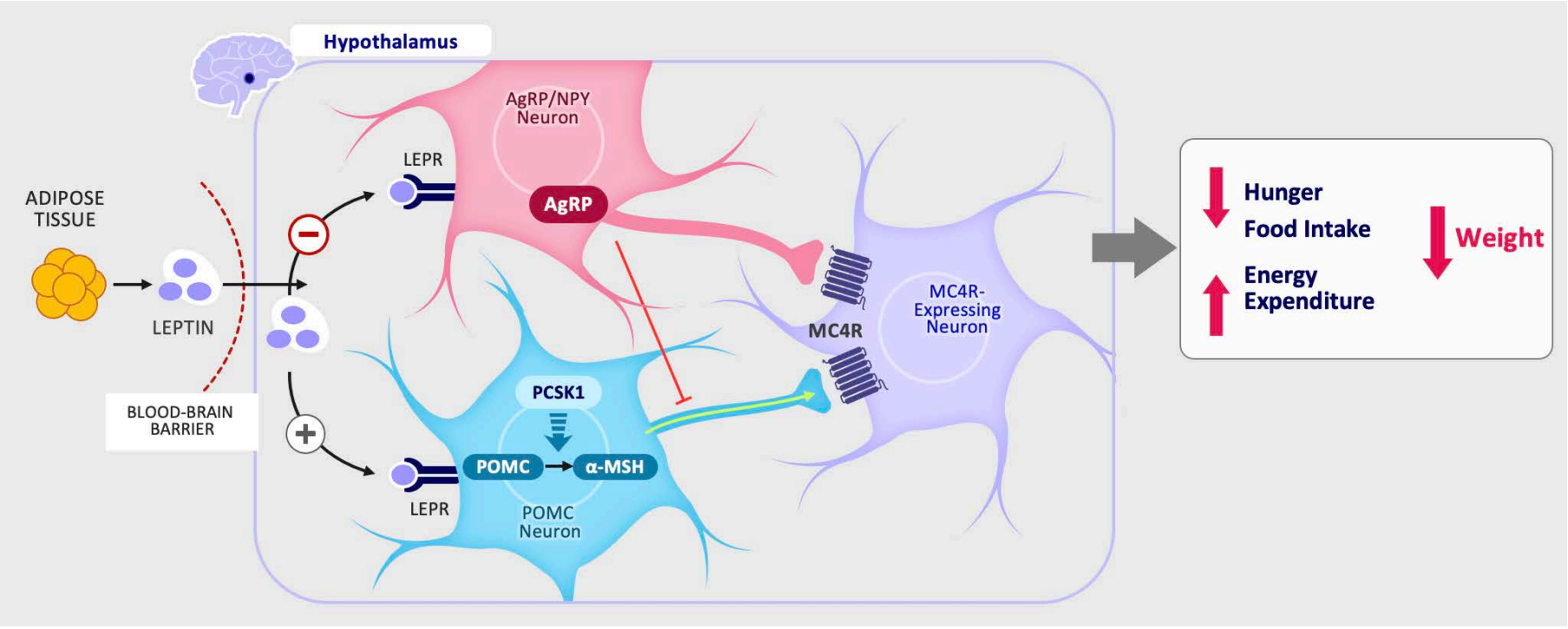
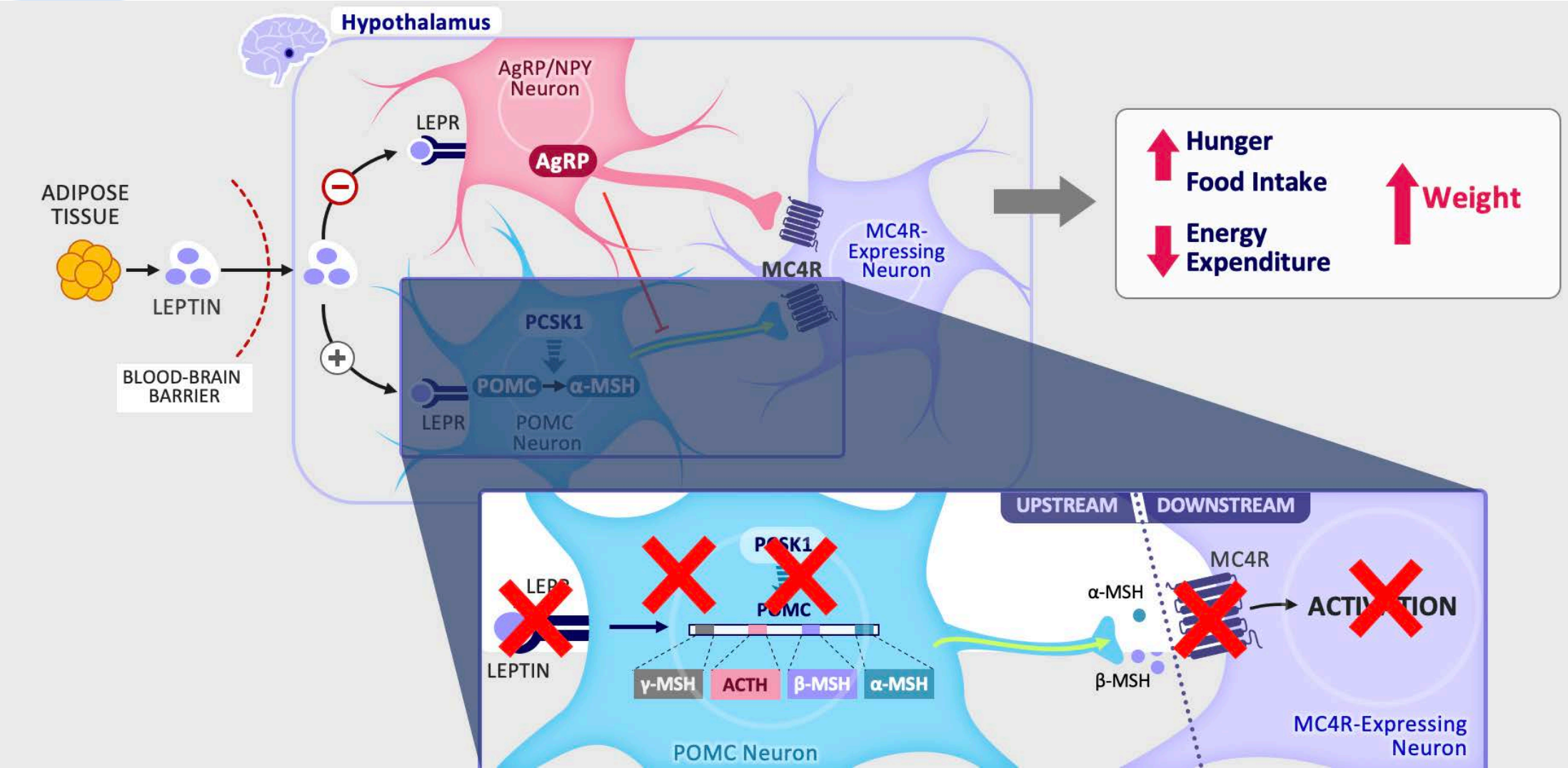


Figure 17. Rhythm

1. Yazdi et al. *PeerJ*. 2015;3:e856. **2.** Heymsfield et al. *Obesity (Silver Spring)*. 2014;22(suppl 1):S1-S17. **3.** Huvenne et al. *Obes Facts*. 2016;9:158-173.
4. Muñoz Yáñez et al. *Austin Journal of Nutrition and Metabolism*. 2017;4:1052.
5. Ahima and Antwi. *Endocrinol Metab Clin North Am*. 2008;37:811-823.
6. Fahrooqi and O'Rahilly. *J Endocrinol*. 2014;223:T63-T70. **7.** Davenport et al. *Curr Biol.* 2007;17:1586-1594. **8.** Seo et al. *Hum Mol Genet*. 2009;18:1323-1331.
9. Heydet et al. *Dev Neurobiol*. 2013;73:1-13. **10.** Bochukova et al. *Nature.* 2011;463: 666-670. 11**.** Burns et al. *Hum Mol Genet*. 2010; 19: 4026-4042.
12. Doche et al. *J Clin Invest*. 2012; 122: 4732-4736. **13.** Yang et al. *Nature Communications*. 2019; 10:1718**.**

Genetic Obesity: Melanocortin 4 Receptor Pathway Dysfunction



Yazdi et al, 2015; Heymsfield et al., *2014;* Huvenne et al., 2016; Muñoz Yáñez et al., 2017; Ahima and Antwi, 2008; Fahrooqi and O'Rahilly, 2014; Davenport et al. , 2007; Seo et al., 2009; Heydet et al., 2013; Bochukova et al., 2011; Burns et al., 2010; Doche et al., 2012; Yang et al., 2019

Figure 18. Rhythm

Genetic Obesity: Bardet-Biedl Case Study

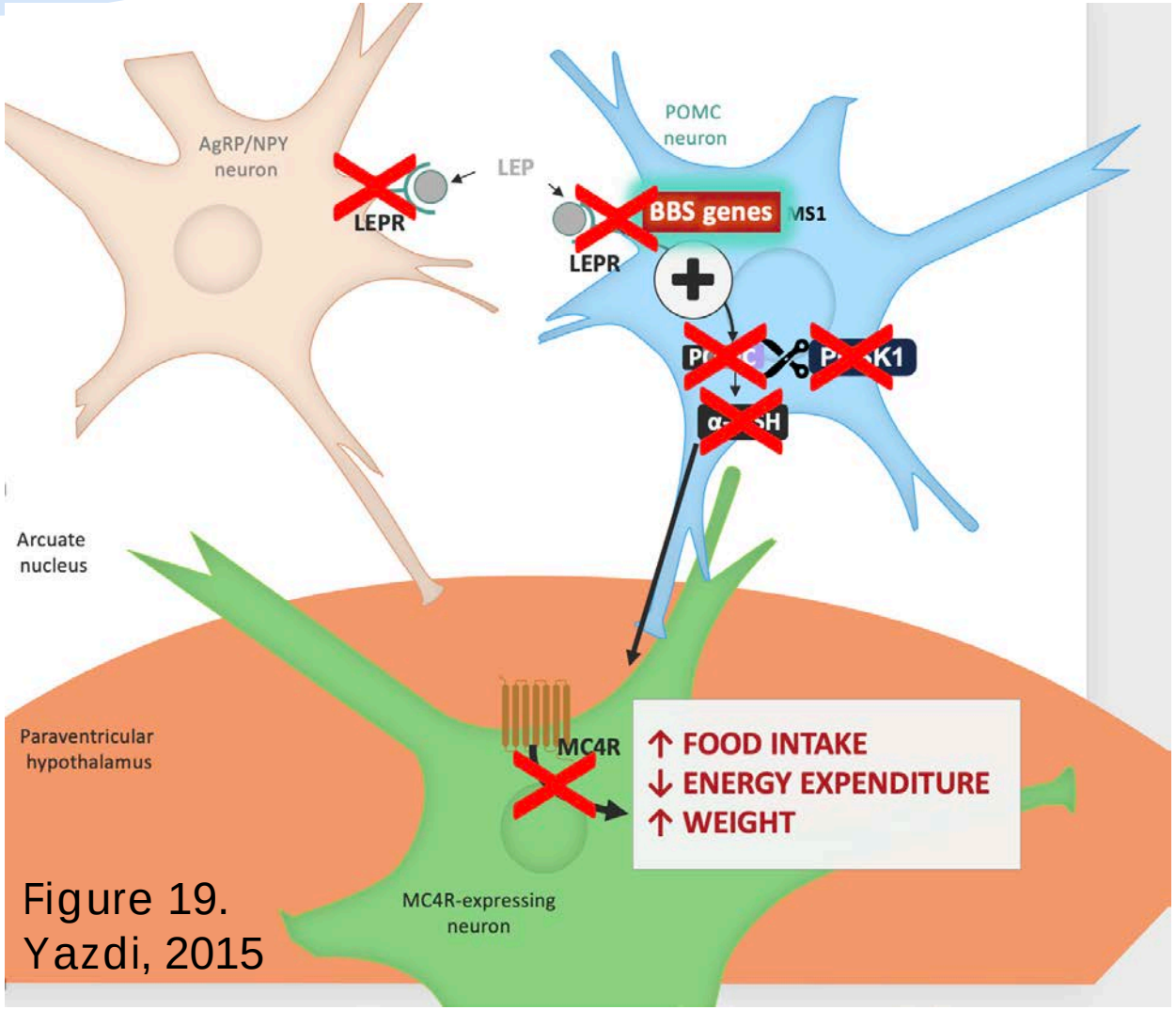


Figure 19. Yazdi, 2015

Figure 20. Istockphoto.com

Example Case Report: Bardet-Biedl Syndrome

- Male patient referred because of severe obesity at 5 years of age (>2x ULN on growth chart)

Family history

- Parents unrelated
- Parents healthy

Patient history

- Surgeries
  - Postaxial polydactyly on left hand
- Rod-cone dystrophy at age 23 years, with gradual vision loss
- Diabetes, dyslipidemia, hypertension, kidney dysfunction, and liver disease manifested by fibrosis, steatosis, hepatomegaly, and NAFLD

Patient diagnosis

- Sequencing
- Homozygous M390R variant in *BBS1*

Diagnosis of BBS

NAFLD, nonalcoholic fatty liver disease; BBS, Bardet-Biedl Syndrome.

Boscolo et al. *J Endocr Soc*. 2017;1:317-322.

Clinical Characteristics of Bardet-Biedl Syndrome

Diagnostic criteria: 4 primary features or 3 primary features plus 2 secondary features[1]

Primary criteria	Frequency	Secondary criteria	Frequency
Rod-cone dystrophy	93%	Speech delay	54%-81%
Polydactyly	63%-81%	Developmental delay	50%-91%
Obesity	72%-92%	Diabetes mellitus	6%-48%
Genital anomalies	59%-98%	Dental anomalies	51%
Renal anomalies	53%	Congenital heart disease	7%
Learning difficulties	61%	Brachydactyly Syndactyly	46%-100% 8%-95%
		Ataxia/Poor coordination	40%-86%
		Anosmia/Hyposmia	60%

Table 7. Forsythe 2013

Forsythe and Beales. *Eur J Hum Genet*. 2013;21:8-13.

Genetic Obesity: Treatment

Setmelanotide

- FDA approved for homozygous POMC, PCKS1, LEPR (PPL), and compound heterozygous BBS
- Other indications and pharmaceutical drugs in the works

Lipoprotein(a) or lp(a)

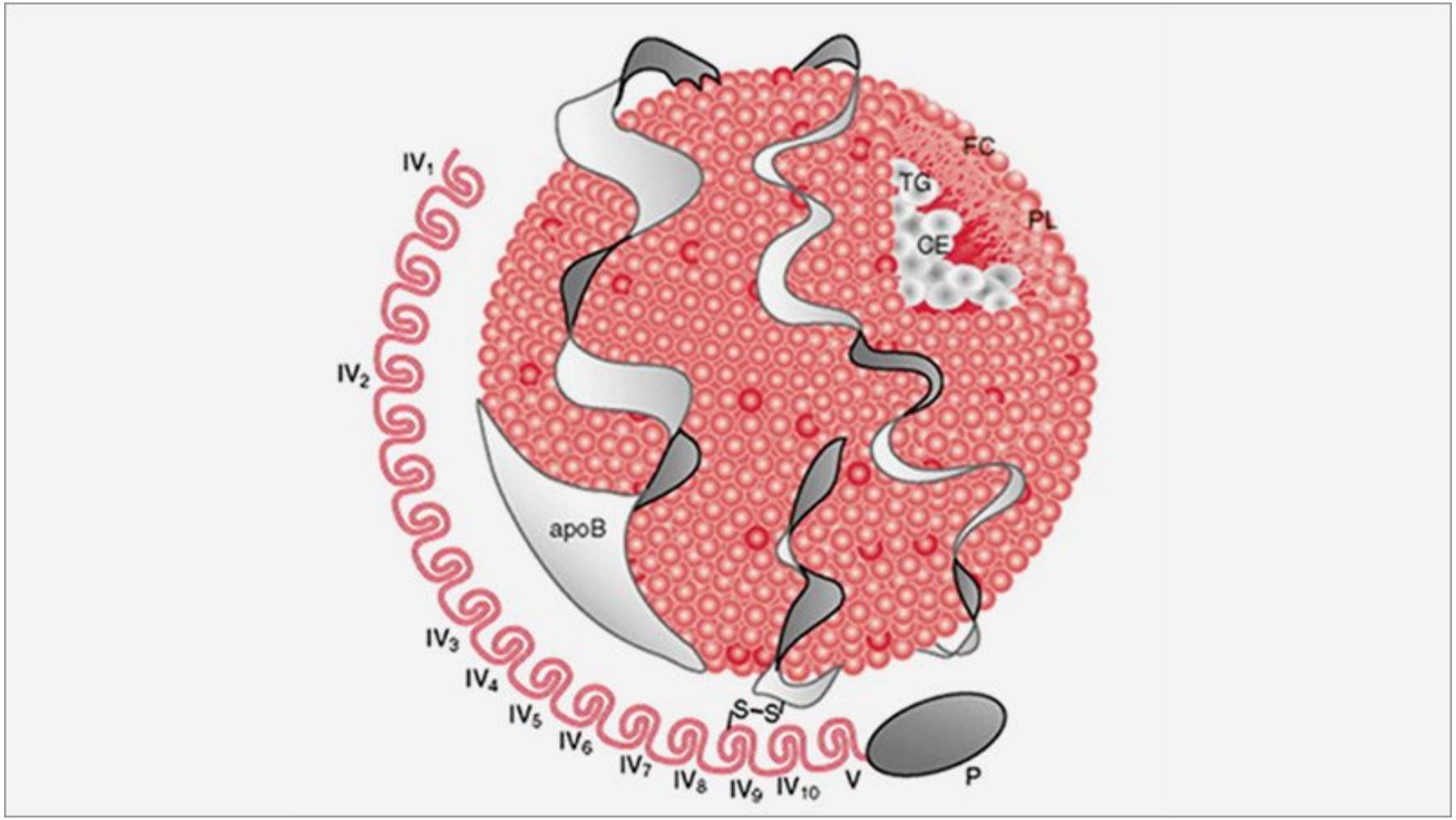
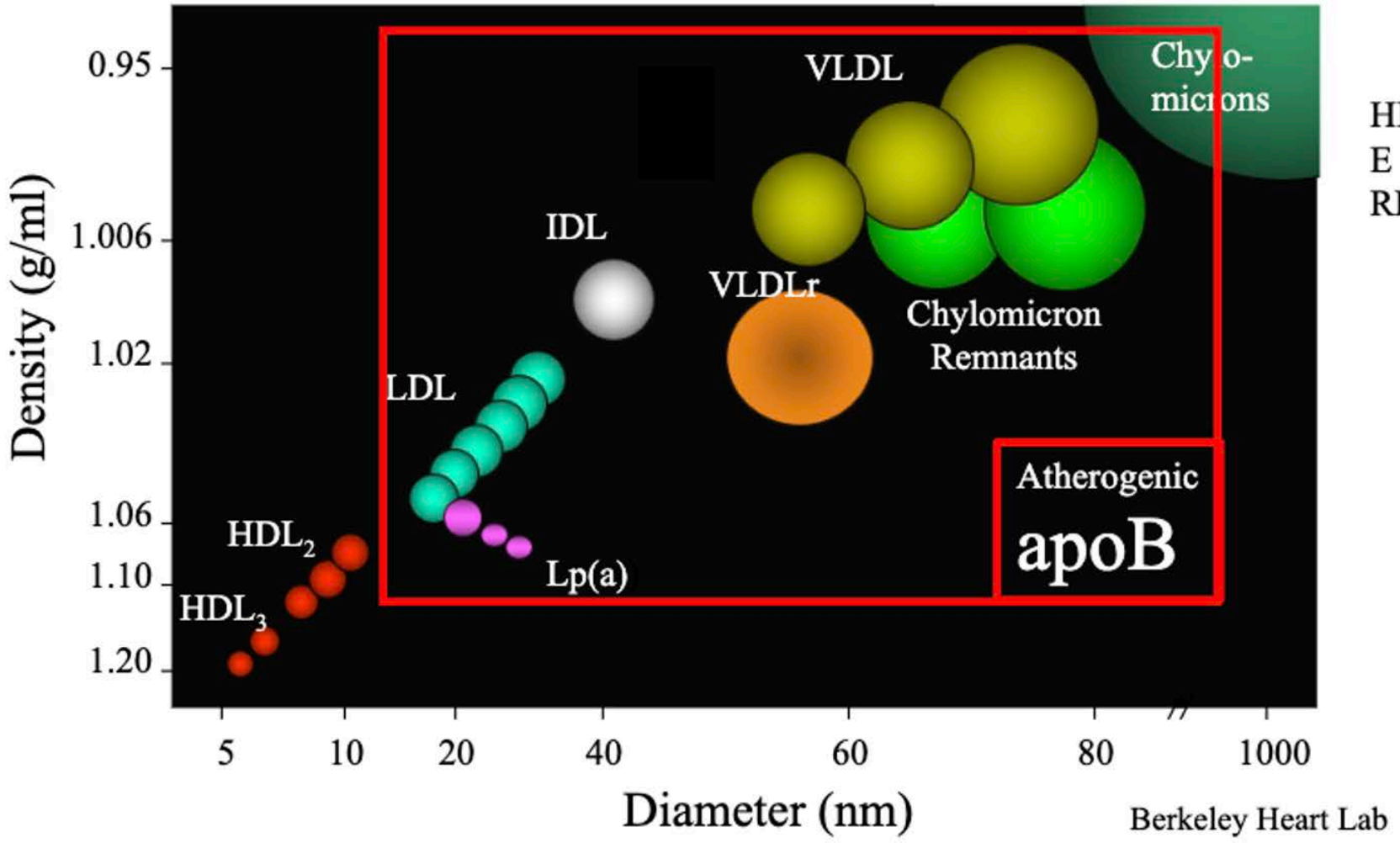


Figure 21. CDC, 2022

Lp(a) is Bound to apoB



HIV 100 nm
E coli = ~2000 nm
RBC = ~9000 nm

Figure 22. NLA Advanced Lipidology

Lp(a): Epidemiology

- High levels (>50 mg/dL or >105-125 nmol/L) present in 20% of the population
- Highest prevalence in Black population
- Begins to be near fully expressed at 2 years of age and is full expressed by age 5
- Phenotypic penetrance may depend on other factors such as high CRP or IL-6

Sources 44-66

Lp(a) Pathogenesis

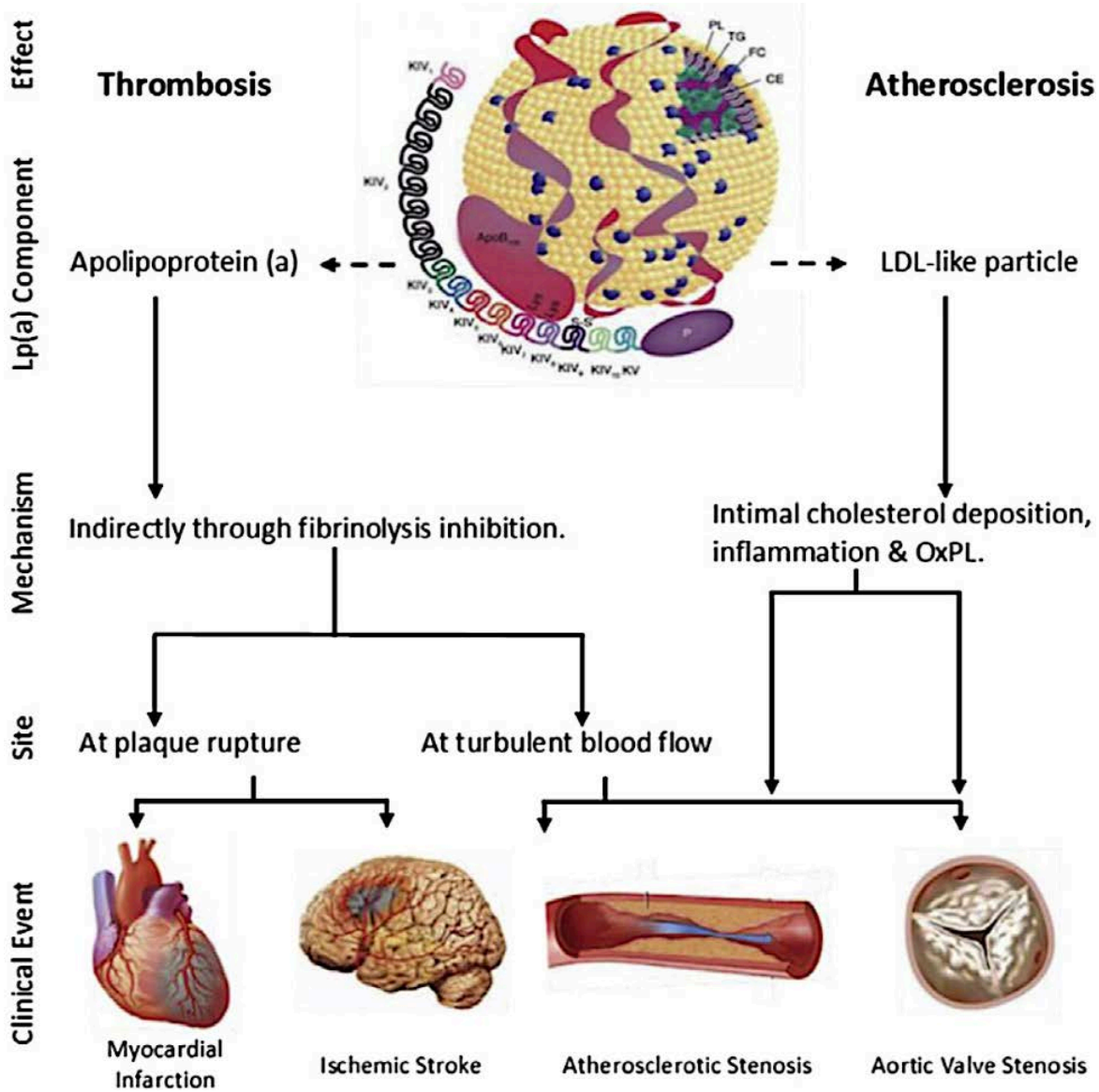


Figure 23. NLA Position Paper Lp(a)

Sources 44-66

Lp(a) Concentration

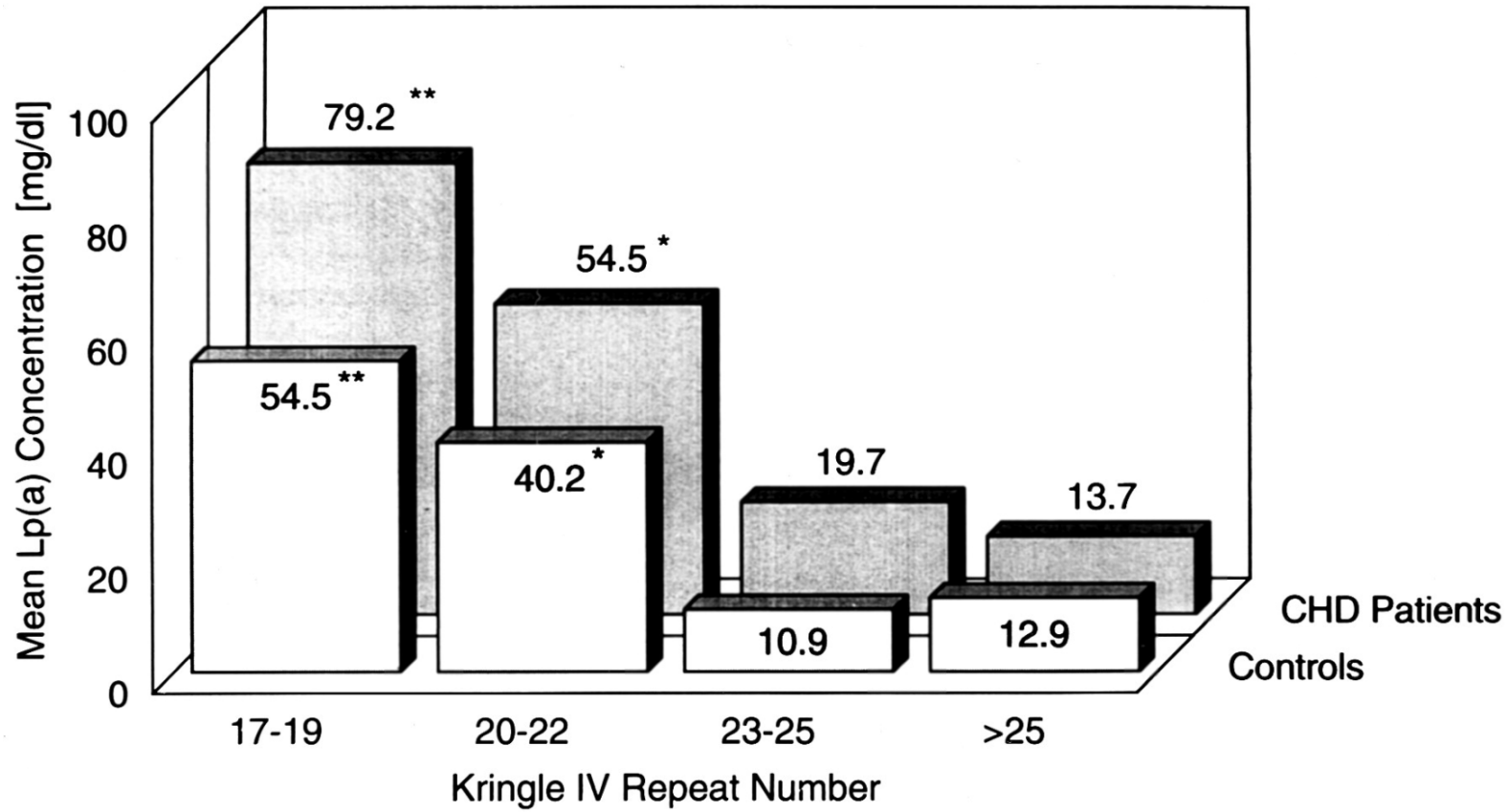


Figure 24. Wilson, 2019

Sources 44-66

Lp(a) Treatment

- Antisense oligonucleotide lower lp(a) by 70-90%
- Apharesis lowers by 30-35%
- Niacin/PCSK9i/CETPi/Mipomersen lower by 20-30%
- Statins may raise about 10%: statins have been shown in the Heart Protection study to still provide protection especially in those with high lp(a) despite the fact it may raise lp(a) because the reduction in apoB is likely more protective by at least a factor of 6 then the rise in lp(a)

Sources 44-66

Lp(a) & Niacin

- European Atherosclerosis Society advises niacin treatment in some patients with high Lp(a).
- AHA/ACC and NLA advise against use of Niacin
- It is believed a decrease of 50 mg/dL is necessary before cardiovascular risk reduction is seen based on genome-wide association studies (over entire lifespan thus current studies are underpowered).
- Levels >170 mg/dl or >350 nmol/L would therefore theoretically benefit from Niacin. Niacin lowers levels by approximately 30%

Sources 44-66

In Summary

- Lipedema may be present in as much as 11% of the female population and diagnosis can lead to early intervention with bariatric surgery or methods to reduce pain (i.e. MLD, compression garments, excise, etc).
- Genetic causes of obesity are RGDO that may be more common than we realize. There are drug treatments available for 4 distinct mutations.
- Lp(a) is the most inheritable risk of cardiovascular disease risk and will likely become the next CVD target in the upcoming future.
- Early diagnosis can improve patients' self-perception by reducing stigma, improve care, reduce a diagnostic odyssey over lifetime, and prepare for future treatments and drug trials.

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Thank you, Questions?