

ENFOQUE CLÍNICO DE LOS ESTADOS COMÓRBIDOS DE LA OBESIDAD

Prof. M. Moya.

Alicante.



Obesity Defined as Excess Storage of Inert Triglycerides – Do We Need a Paradigm Shift?

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PRONÓSTICO DE LA OBESIDAD PEDIÁTRICA

- No causa de muerte en edad pediátrica
- Alteraciones presentes : S Metabólico, Insulin resistencia, hígado graso, apnea...
- No causa de ECV en el adulto si se cura
- Consecuencias socioeconómicas :
 - Menos años de estudio
 - Menor número de matrimonios
 - Menor ingreso económico

TRACKING

Niños ≤ 10 años, si (Z-score)  ADULTO OBESO

Subpeso	(-0.6 SD)	_____	11%
Normopeso	(+0.5 SD)	_____	36%
Sobrepeso	(+1.3 SD)	_____	59%
Obeso	(> 2 SD)	_____	87%
Adolescente obeso		_____	90%

Niño obeso < 3 y _____ no riesgo añadido

-
- Bogalusa Heart Study 2005, 2009
 - Singapore
 - EU

PEDIATRIC OBESITY PRESENT LURE: CO-MORBIDITIES

Adult

- Metabolic Syndrome (MetS)



- Cardiovascular disease (CVD)

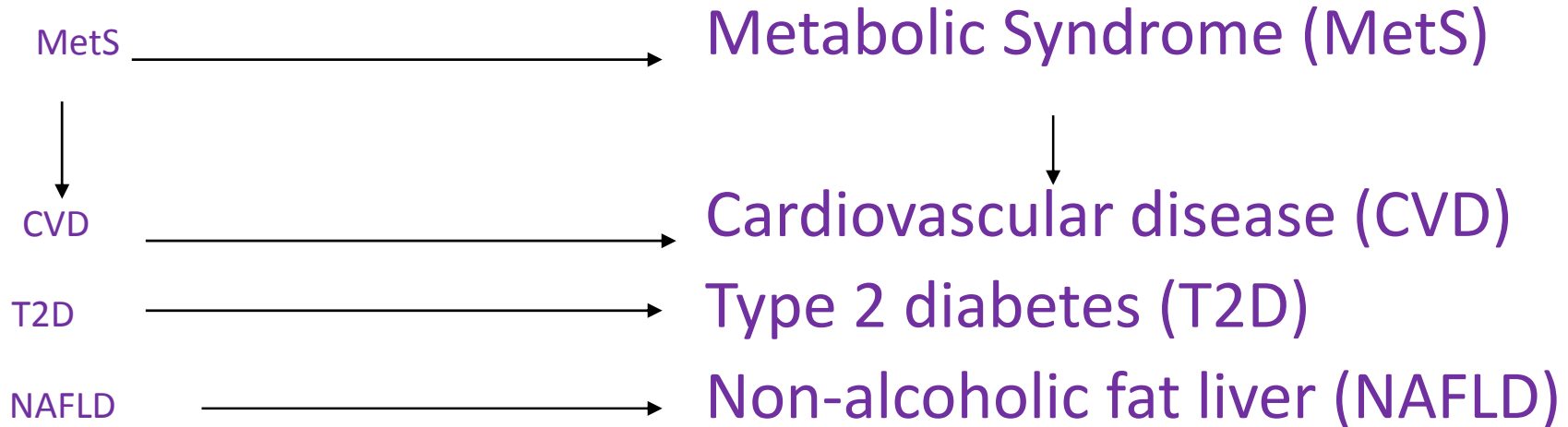
- T2D

- Non-alcoholic fat liver (NAFLD)

PEDIATRIC OBESITY PRESENT LURE: CO-MORBIDITIES

Pediatric ages

Adult



Early diagnosis ≈ Better prevention

SÍNDROME METABÓLICO PEDIÁTRICO

. **OBESIDAD TRONCAL** + 2 componentes :

TG >150 mg/dL; **HDL-C** <40 mg/dL; **Hipertensión** > 130/85 mmHg, **Glucemia** en ayunas >100mg/dL

. La obesidad troncal es un factor independiente para la insulín resistencia.

EL MetS ES UNA SITUACIÓN SUBCLINICA QUE IDENTIFICA AL NIÑO/ADOLESCENTE OBESO CON RIESGO DE COMORBIDADES ACTUALES O FUTURAS

Zimmet P et al. Pediatr Diabetes 2007; 8:299 (IDF)

ADULTO

*Síndrome Metabólico

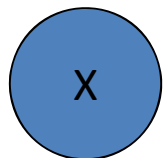
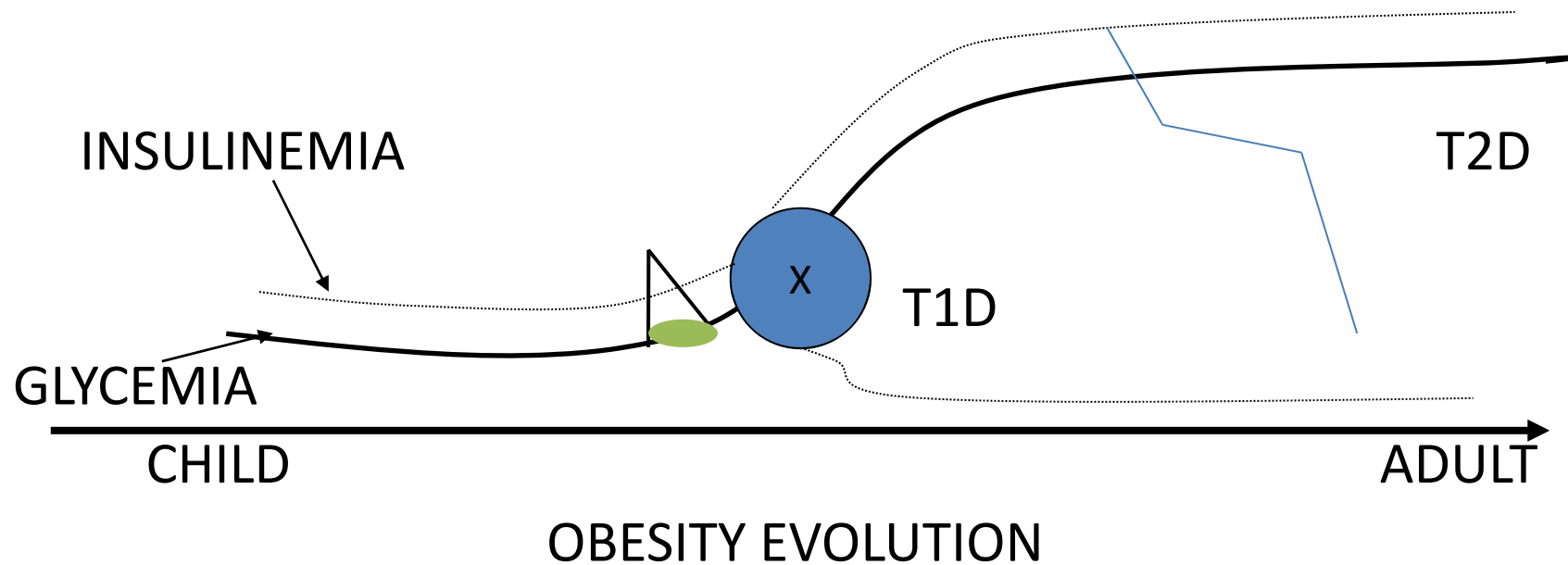
1. Obesidad central: cintura > 94 cm
2. Alt Met Glucosa: G ayunas >100 mg /dL
3. Dislipemia: TG > 150 mg/dL
4. HDL-C < 40 (50 ♀) mg/dL
5. Hipertensión > 130/ 85 mmHg

* Estados comórbidos de la obesidad

- Diabetes T2
- ECV
- HG No Alcohólico
- Hiperuricemia
- -
- -

IR

Insulin resistance development throughout childhood



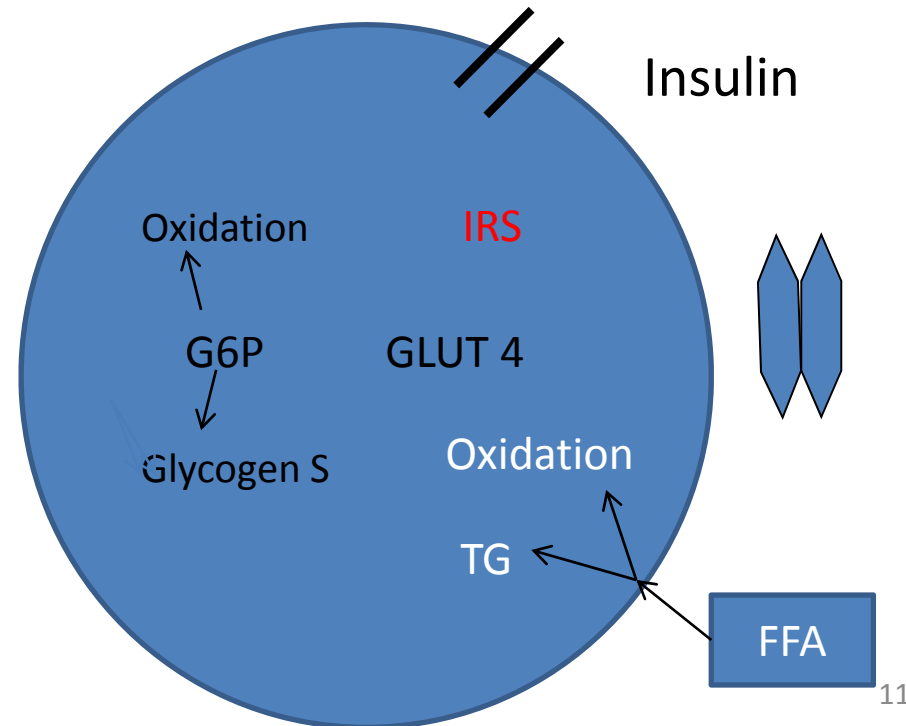
Starting point can move toward an earlier age if genetically predisposed

OBESIDAD CENTRAL → INSULÍN RESISTENCIA →
→ ESTADOS COMÓBIDOS

IR MECHANISMS IN LIVER AND MUSCLE CELLS

Normal caloric intake implies Intra myo/hepatic transport:

- Glucose: GLUT 4
- Fat: saturable



G Shulman
New Haven

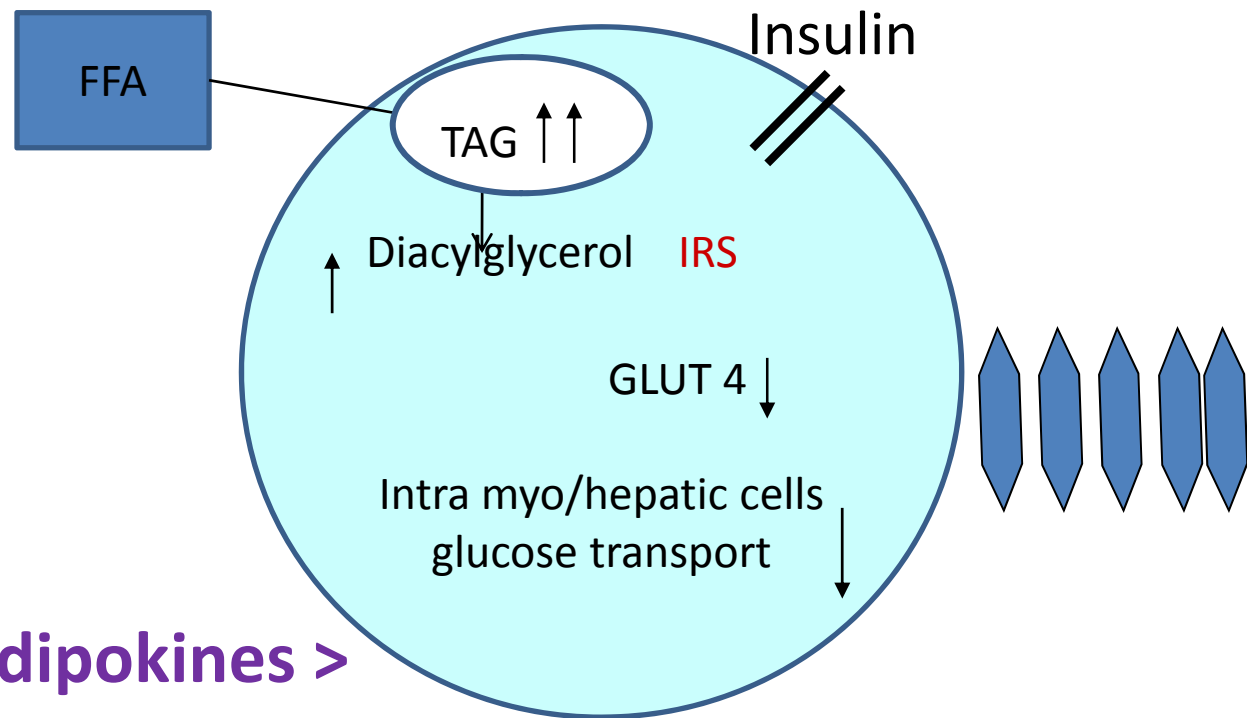
PLASMA NEFA (mmol/L):

		Normal weight	Ob	P
	TOTAL	332	422	.01
14:0	Myristic	9	13	.003
16:0	Palmitic	129	165	.01
18:1 n-9	Oleic	143	191	.009
18:0	Stearic	48	50	-

Weiss R, 2010

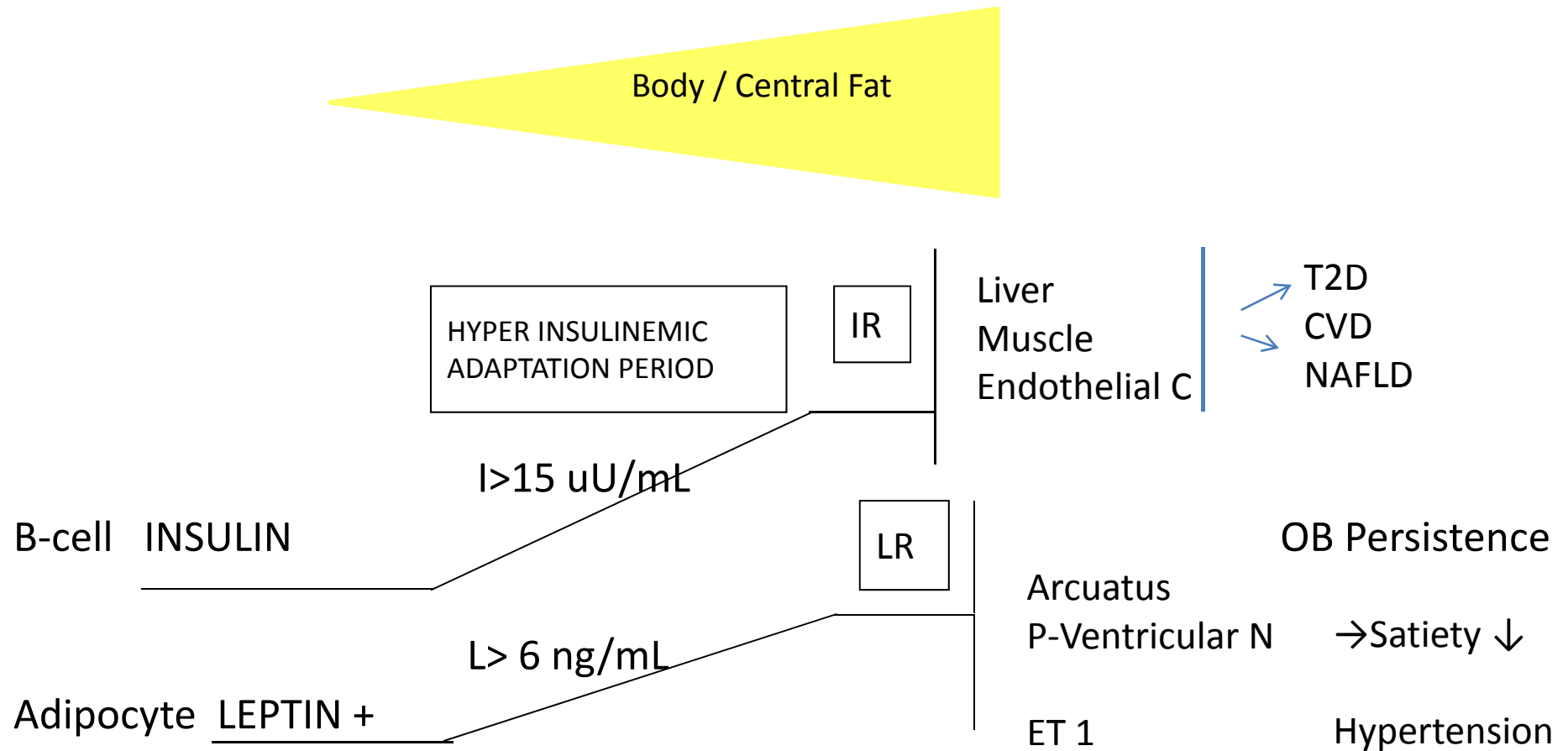
IR MECHANISMS IN LIVER AND MUSCLE CELLS

ORIGIN: Extra caloric intake



ORIGIN: Adipocyte
Proinflammatory adipokines >
Adiponectin <

VISCERAL FAT PROVED CONSEQUENCES



CONSECUENCIAS DE LA OBESIDAD CENTRAL

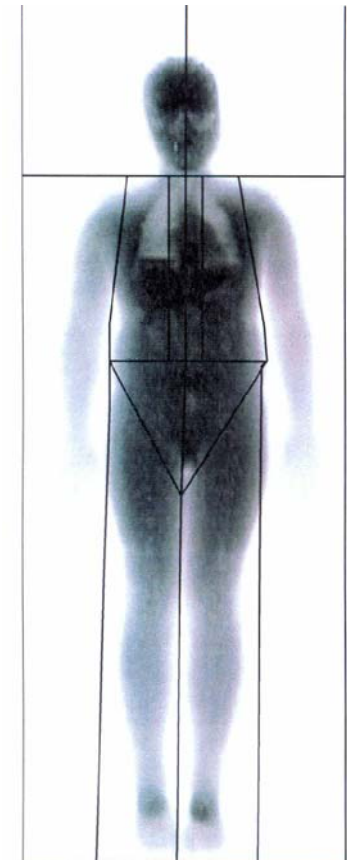
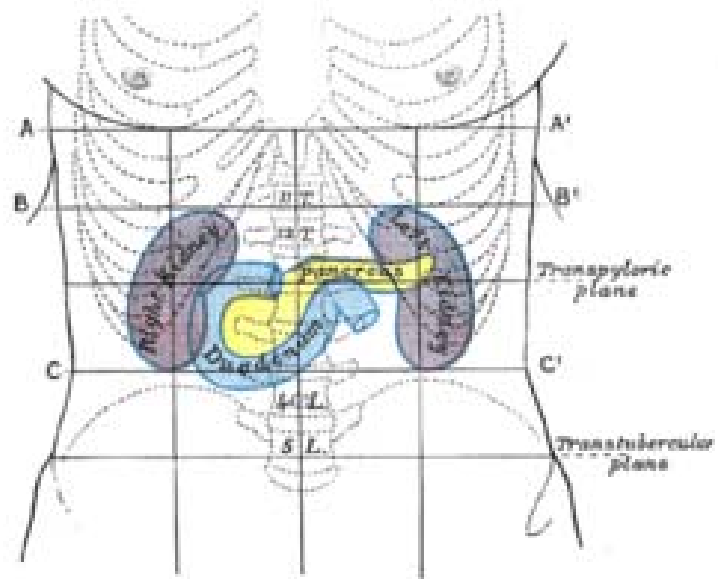
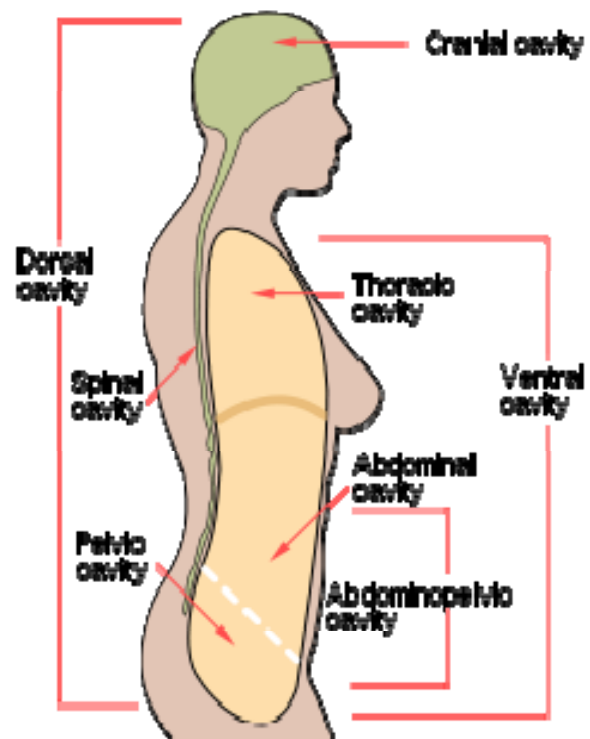
los adipocitos de la obesidad central son un factor clave para MetS y el desarrollo de la IR.

La persistencia de la obesidad central desde la niñez hasta edad adulta, favorece la aparición de T2D, CVD and NAFLD

S. Lee. 2006

S. Lee. 2006

TRUNK FAT



GRASA VISCERAL se localiza en la cavidad abdominal entre :

Estómago

Hígado

Vesícula biliar

Bazo

Páncreas

Intestine delgado y mesenterio

Intestino grueso

Grasa perinéfrica y epididimaria

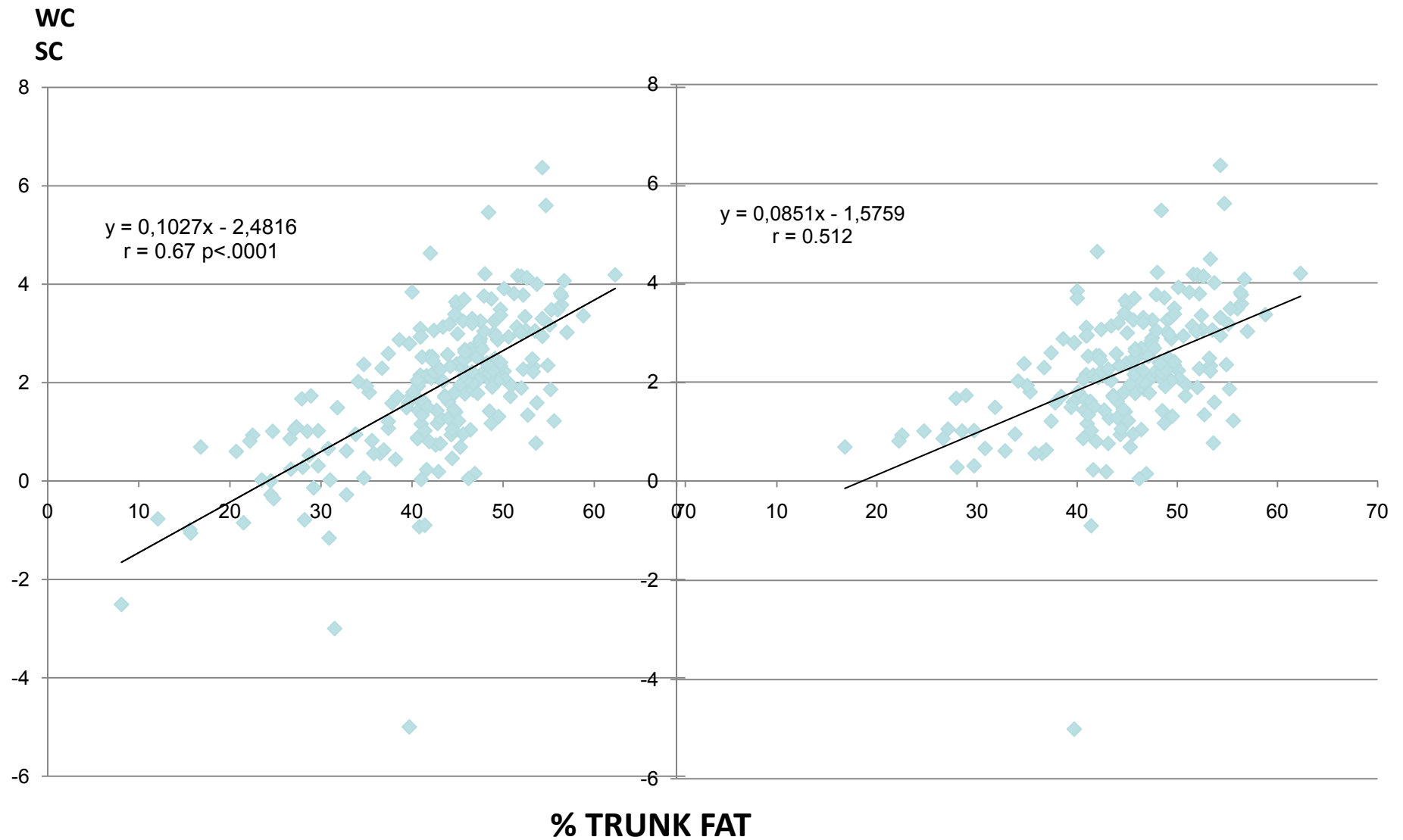
GRASA SUBCUTÁNEA considers also:

Caderas

Nalgas

Muslos

**CORRELATION BETWEEN WAIST CIRCUMFERENCE (WC) AND DXA % TRUNK FAT IN A
POPULATION OF 4.4-17.2 YEARS (n= 196). HUSJ**



$r = 0.669$; $p < 0.0001$

CENTRAL ADIPOSITY (WC and DXA) IN OVERWEIGHT AND OBESE CHILDREN. Initial values (mean (SD))

	OVERWEIGHT (n=19) BMI-zs 1.0 - 1.9	p=	OBESE(n=127) > 2.0
BMI-zs	1.5 (0.3)	.0001	3.5 (1.3)
rBMI %	121.0 (5.0)	.0001	147.8(16.0)
WC-zs	0.98(1.7)	.0001	2.56(1.0)
%Trunk fat	37.4(7.4)	.0001	46.8(6.1)

40%

PARAMETROS 'METABOLICOS' IN NIÑOS Y ADOLESCENTES CON UNA GRASA TRONCAL (%) ≥ 40 (n=53)

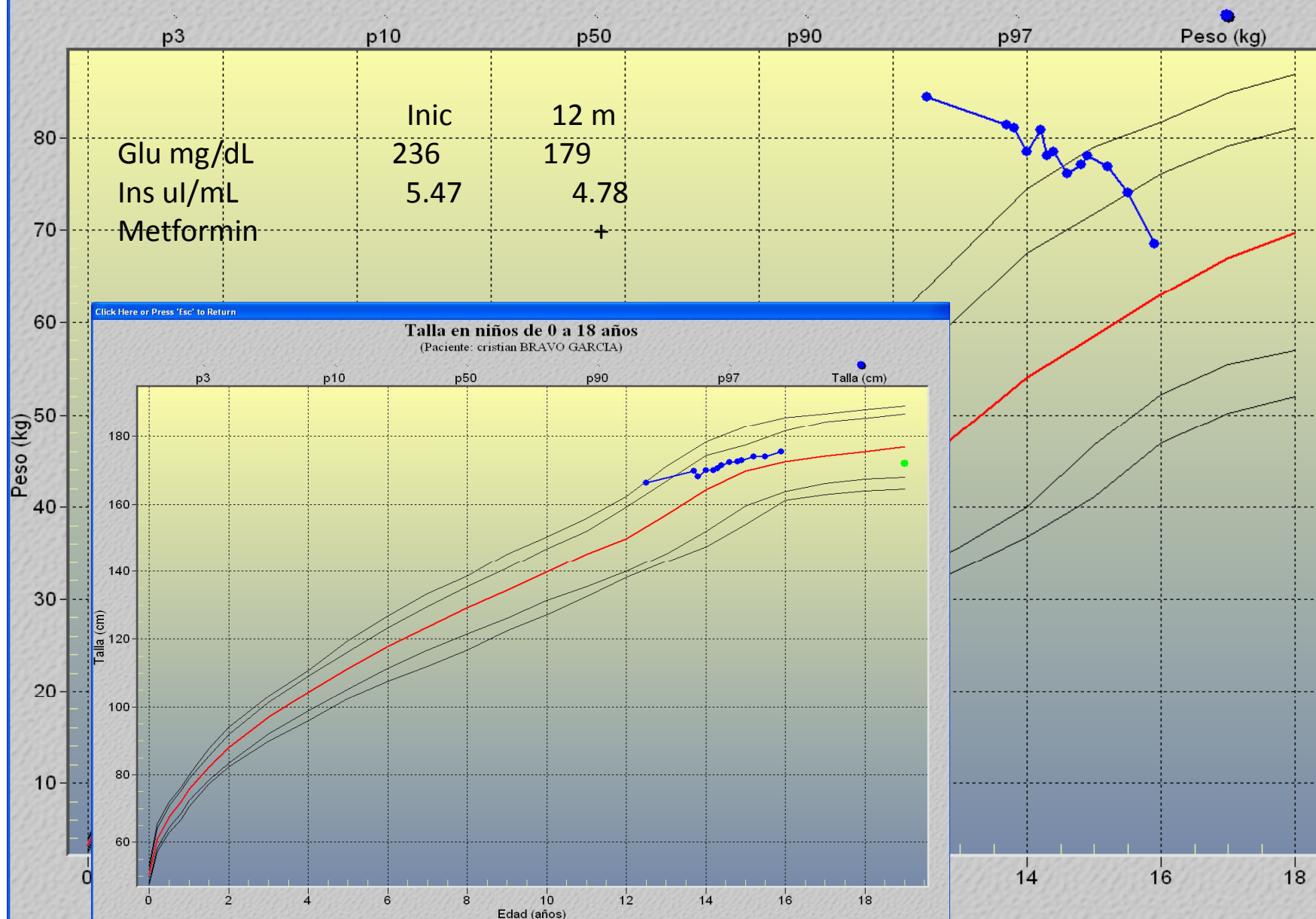
	mean (SD)	n of casos sobre umbral IDF
1. TG (mg/dL)	80 (40)	4
2. HDL-c (mg/dL)	50 (11)	10
3. Glycemia (mg/dL)	94 (23)	5
4. Blood pressure D (Torr)	63 (7)	0
5. Insulinemia (uU/mL)	13 (8)	3
6. Uricemia (mg/dL)	5 (1)	

METABOLIC SYNDROME : 19 CASES

Click Here or Press 'Esc' to Return

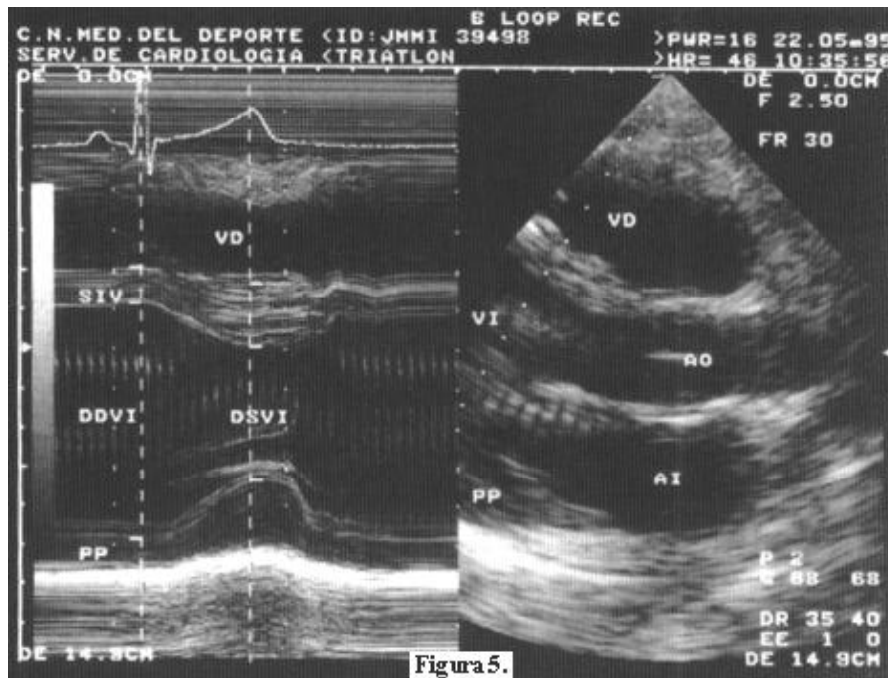
Peso en niños de 0 a 18 años

(Paciente: cristian BRAVO GARCIA)

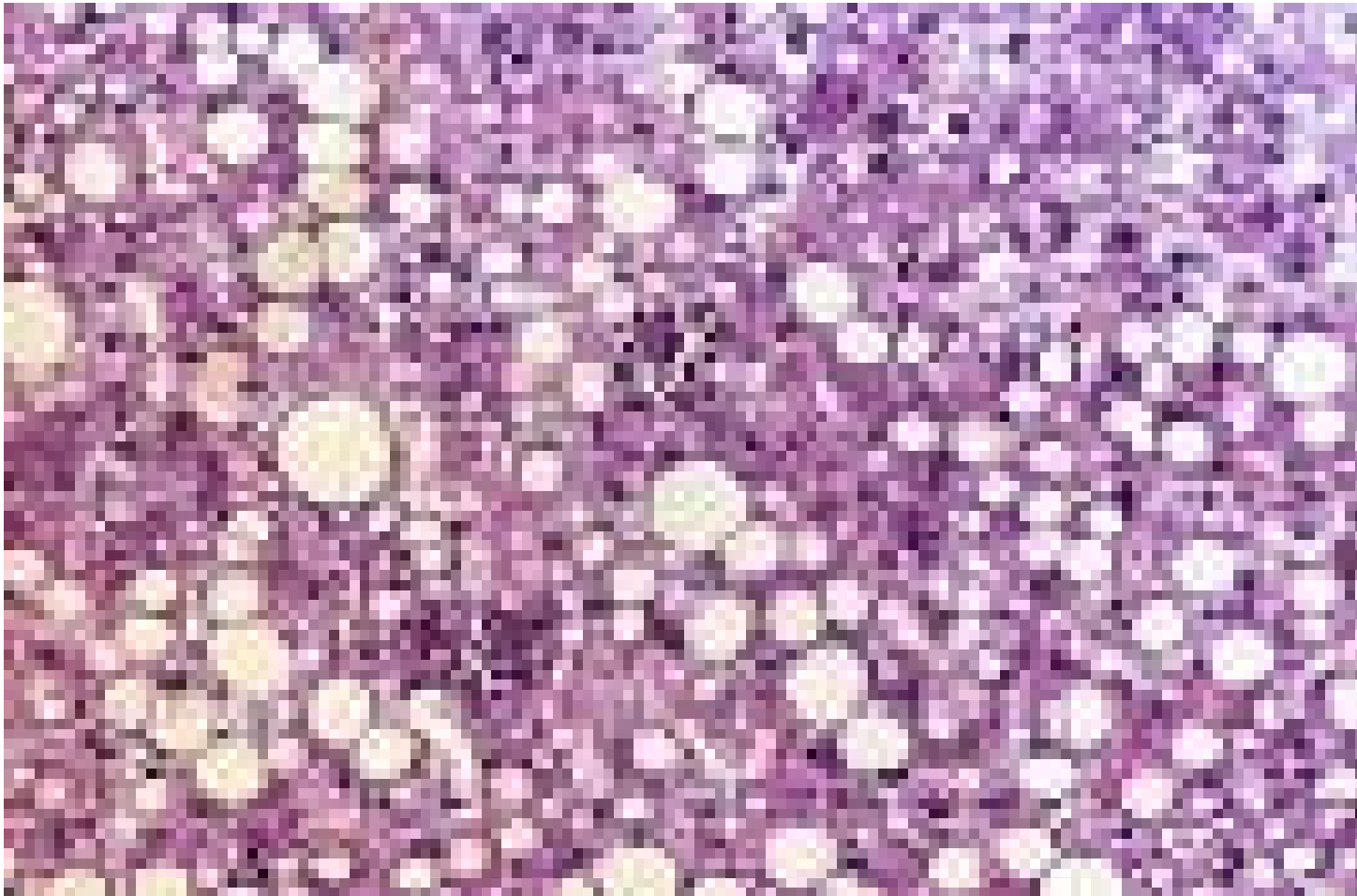


US STRUCTURAL MEASUREMENT AND LEFT VENTRICULAR FUNCTION IN OBESE CHILDREN. HUSJ

US TELESYSTOLIC/DIASTOLIC MEASUREMENTS AND LEFT VENTRICULAR FUNCTION IN OBESE CHILDREN (n=101) AND CONTROLS (n=38)



	OB	CONTR	P<
IV septum thickness (mm)	9.1	7.4	0.05
LVED mm	43,3	39.4	0.05
LV mass height related (g)	38,5	32,8	0,05



HÍGADO GRASO NO ALCOHÓLICO (HGNA)

NONALCOHOLIC FAT LIVER DISEASE (NAFLD)

Es una comorbidad de la obesidad causada por una acumulación macrovesicular de grasa en el hepatocito, agravada por la hiperinsulinemia y con una progresión hacia la esteatohepatitis no bien comprendida e impredecible

CM Orsi

Current opin Endocr 2011; 18:14-22

OVERWEIGHT TRENDS

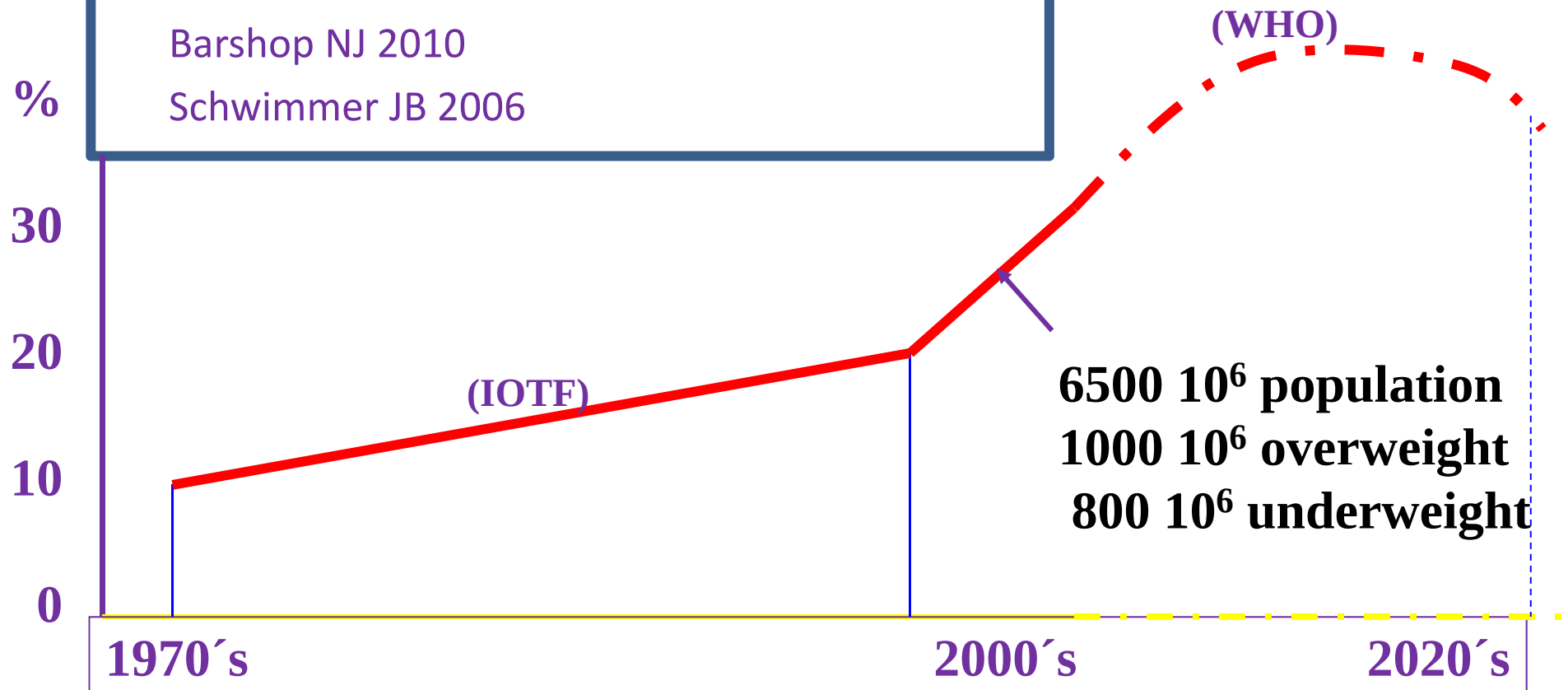
NAFLD. EPIDEMIOLOGY

US + AST/ ALT 10-77%

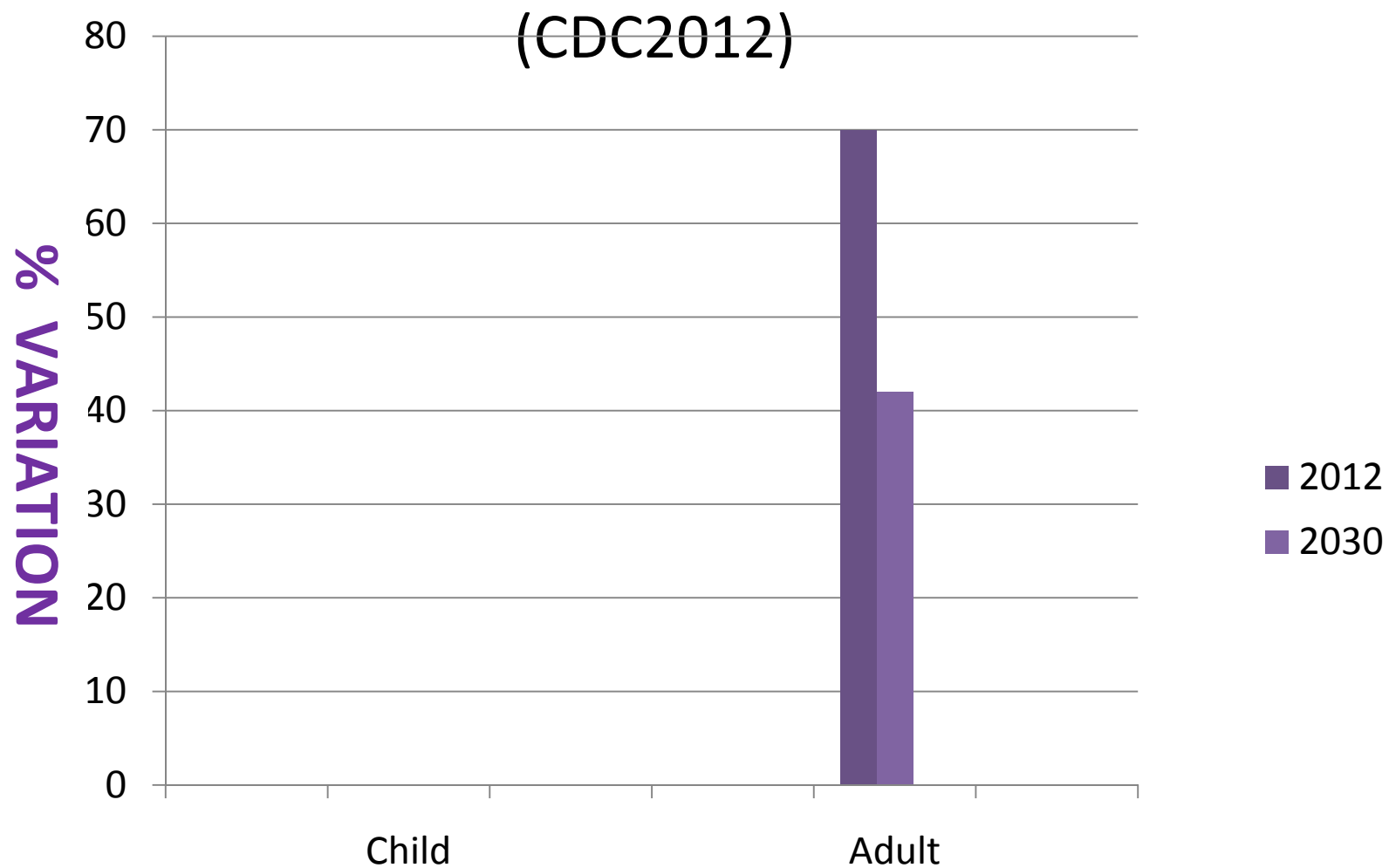
Autopsy (742 children) 9.6%

Barshop NJ 2010

Schwimmer JB 2006



OVERWEIGHT INCREASING RATES



HGNA. ETIOLOGÍA

CAUSAS DE OBESIDAD + :

* Adiposidad visceral

* MC4R (GWA,15 loci)

* ?

PL OXIDATION



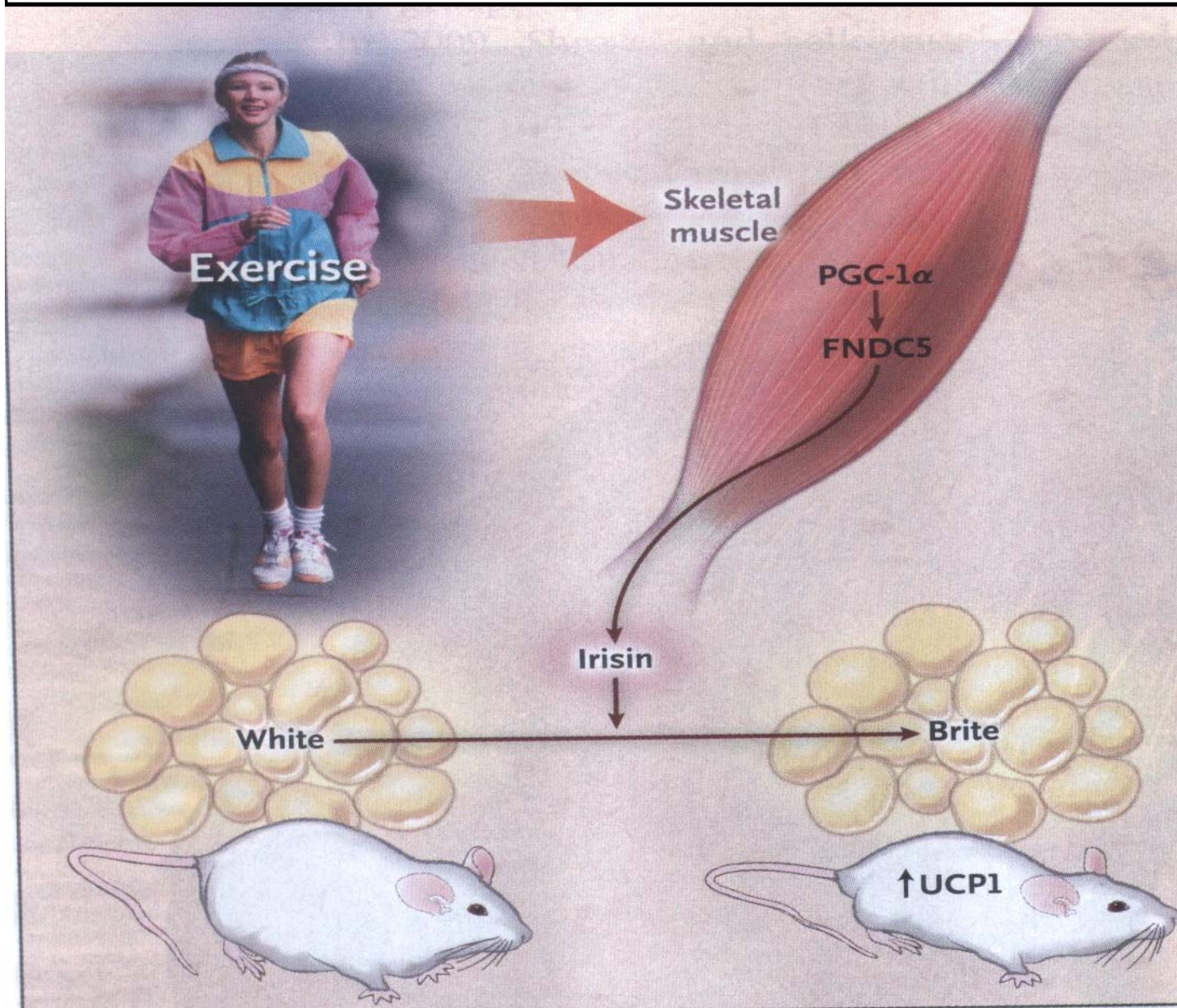


Figure 1. Cross-Talk between Muscle and Fat.

... suppression of peroxisome proliferator...

HGNA. DIAGNÓSTICO

-**CLÍNICA:** Hepatomegalia (?); Cintura > 2SD; Hª familiar

-**BQ:** AST/ ALT, Gamma GT (especificidad <)

-**RM:** Adulto, alta correlación con biopsia

Niño, (fat fraction) Esteatosis > 8.7 %

-**US:** Es el método más usado. Detecta esteatosis > 30 %.

Score 3: ecogenicidad hígado; hepato renal; vasos hepáticos

Elastografía: seguimiento fibrosis hepática

BIOPSIA HEPÁTICA

(‘Patrón oro’ del HGNA)

ESTEATOSIS: Cuando el contenido hepático de TG es superior al 95 centil (~55mg/ g de hígado)

ESTEATOSIS: Cuando más del 5 % de los hepatocitos contienen gúttulas grasas de diámetro igual o mayor al del núcleo

NAFLD. PATIENTS FROM THE METABOLIC UNIT HOSPITAL UNIV. S. JUAN

CRITERIA FOR LIVER BIOPSY:

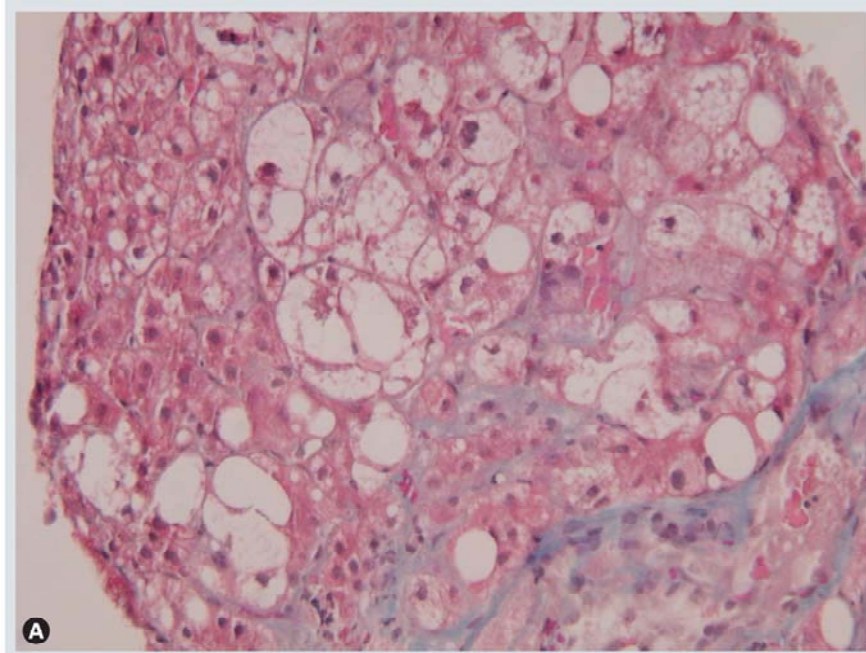
*Trunk fat > 40%

*AST, γ GT, ALT

*Fasting insulinemia > 15 uU/mL

*(Smooth muscle ab)

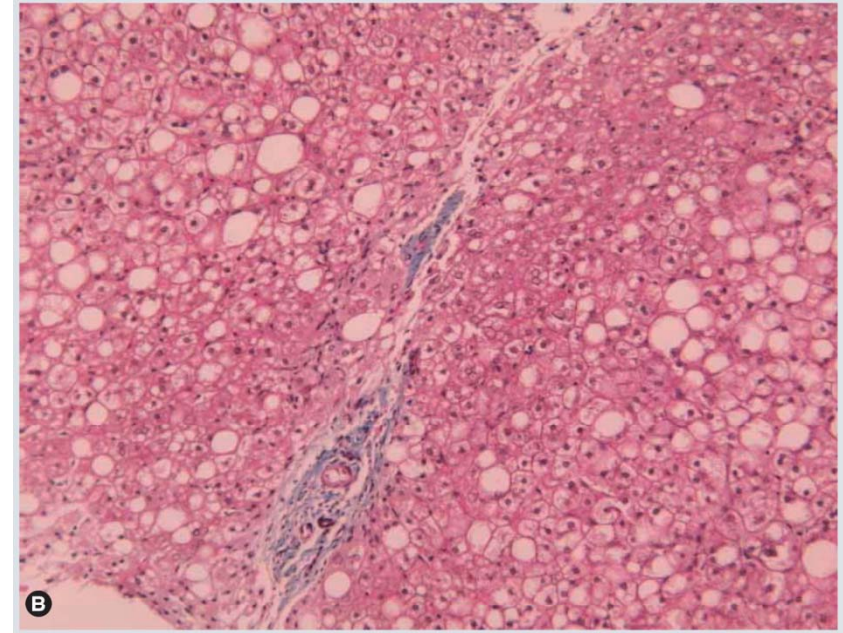
7 CHILDREN



TYPE 1

Macrovesicular steatosis

Ballooning degeneration
And/or perisinusoidal fibrosis
PMN infiltration



TYPE 2

Macrovesicular steatosis
+ portal inflammation

-

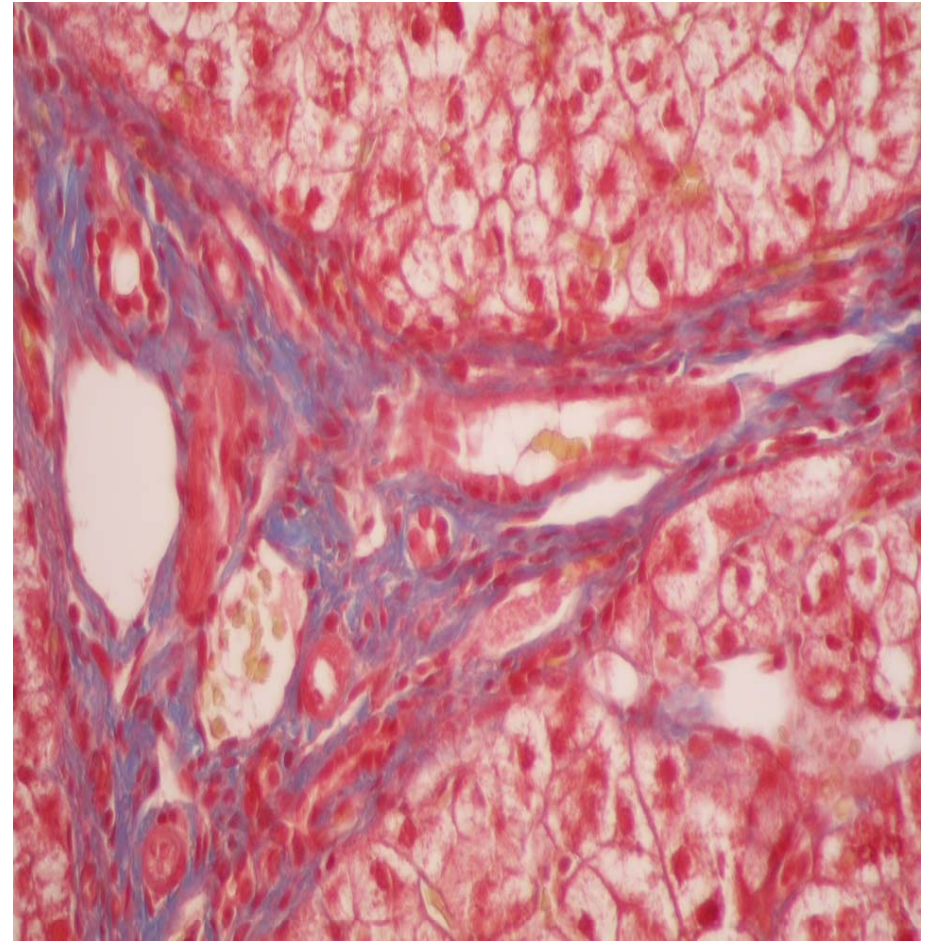
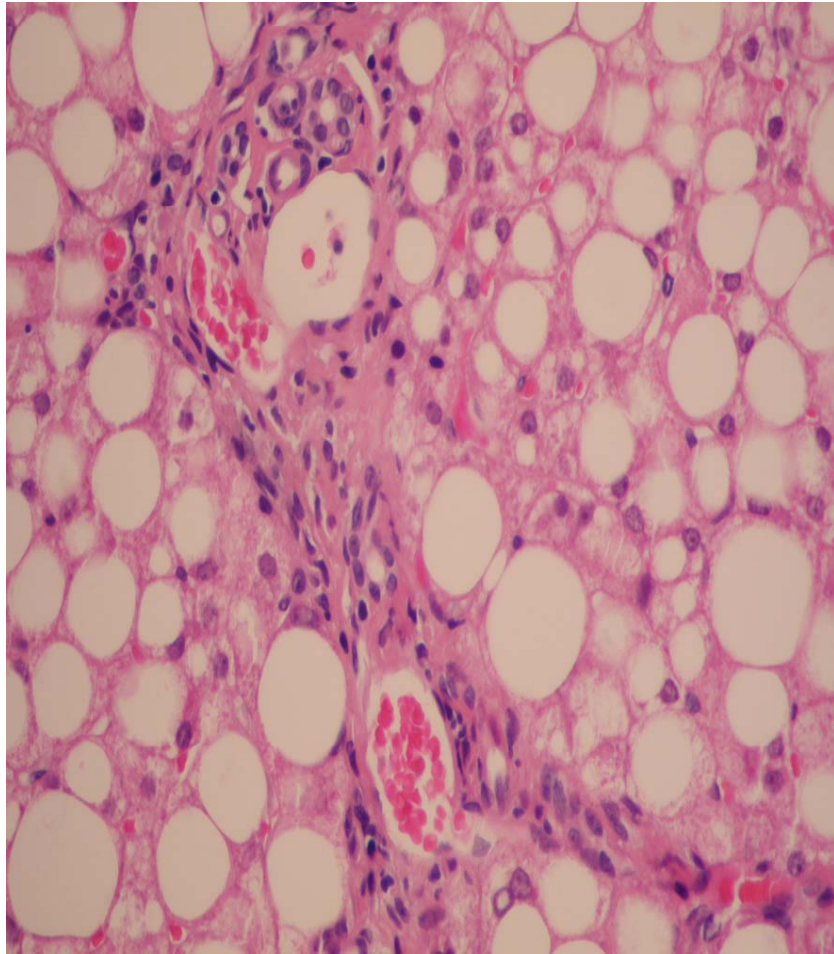
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Periportal MN infiltration

HGNA HISTOPATOLOGÍA

(n=7)

- TIPO 1.....
- TIPO 2.....5
- NASH.....1
- OTRO1 (Wilson)



NAFLD. EVOLUTION (1 year)

TREATMENT: Diet; PA; Lifestyle, for all
Only one Metformin

BMI- zs (and DXA) improvement 3/6

US hepatic fat improvement 1/6

No change 3/6

MAIN FASTING BIOCHEMICAL DATA

	CONTROL (n=27)		CLA (n=26)	
	INITIAL	FINAL	INITIAL	FINAL
Glucose mg/dl	89 (6)	89 (6)	99 (33)	96 (24)
Insulin uU/ml	11.0 (6.0)	12.3(5.5)	15.4 (9.6)	14.7 (7.6)
Hb A _{1c} %	5.6 (.3)	5.3 (.2)*	6.1 (1.5)	5.8 (0.9)
		ns		ns

Mean(SD)

Paired T test (* p=0.022)

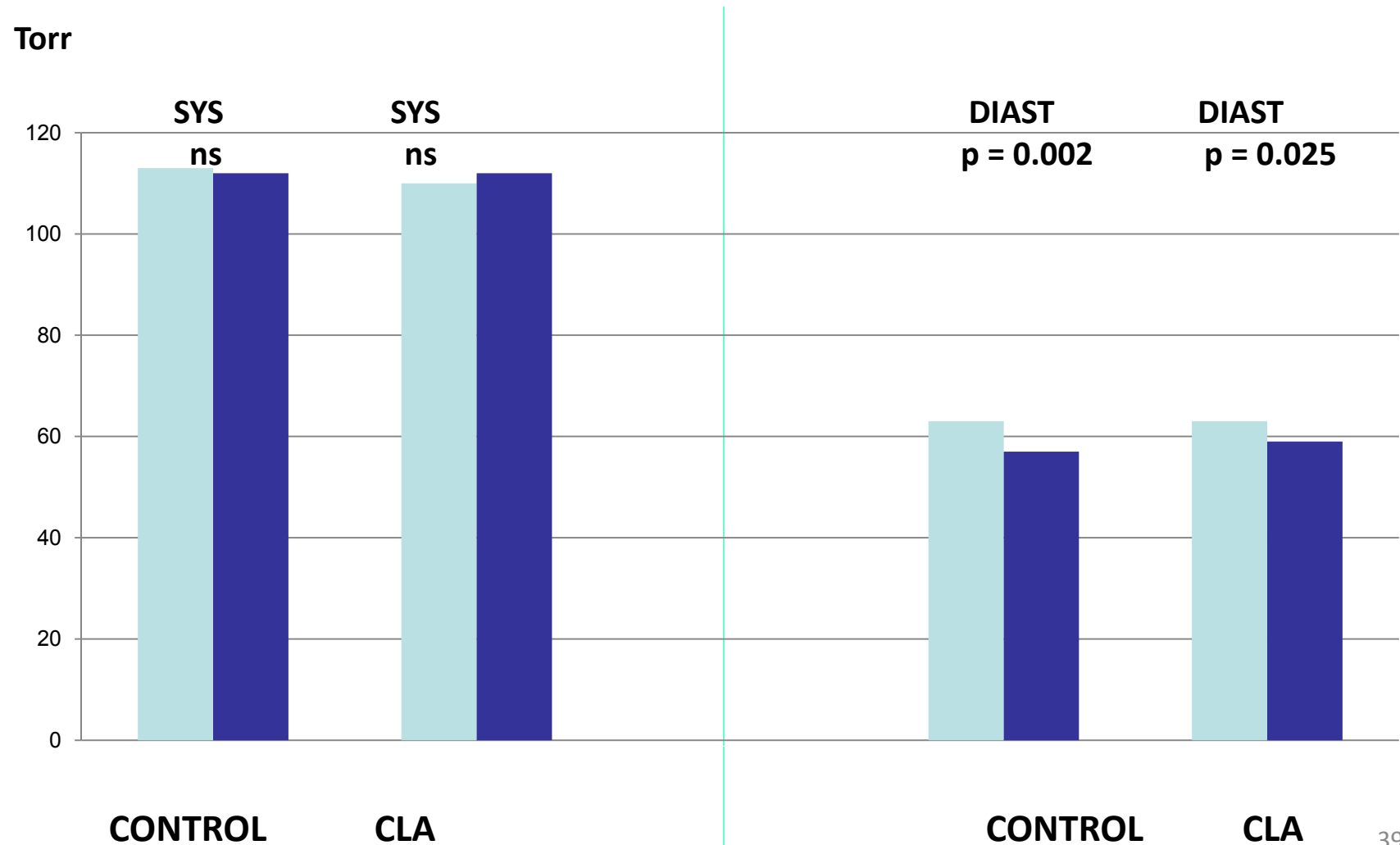
MAIN FASTING BIOCHEMICAL DATA

	CONTROL (n=27)		CLA (n=26)	
	INITIAL	FINAL	INITIAL	FINAL
T Chol mg/dL	157 (29)	159 (25)	163 (32)	162 (36)
HDL mg/dL	48 (11)	53 (10)	50 (10)	51 (12)
TG mg/dL	76 (46)	86 (48)	91 (43)	80 (29)
	ns		ns	

m (SD)

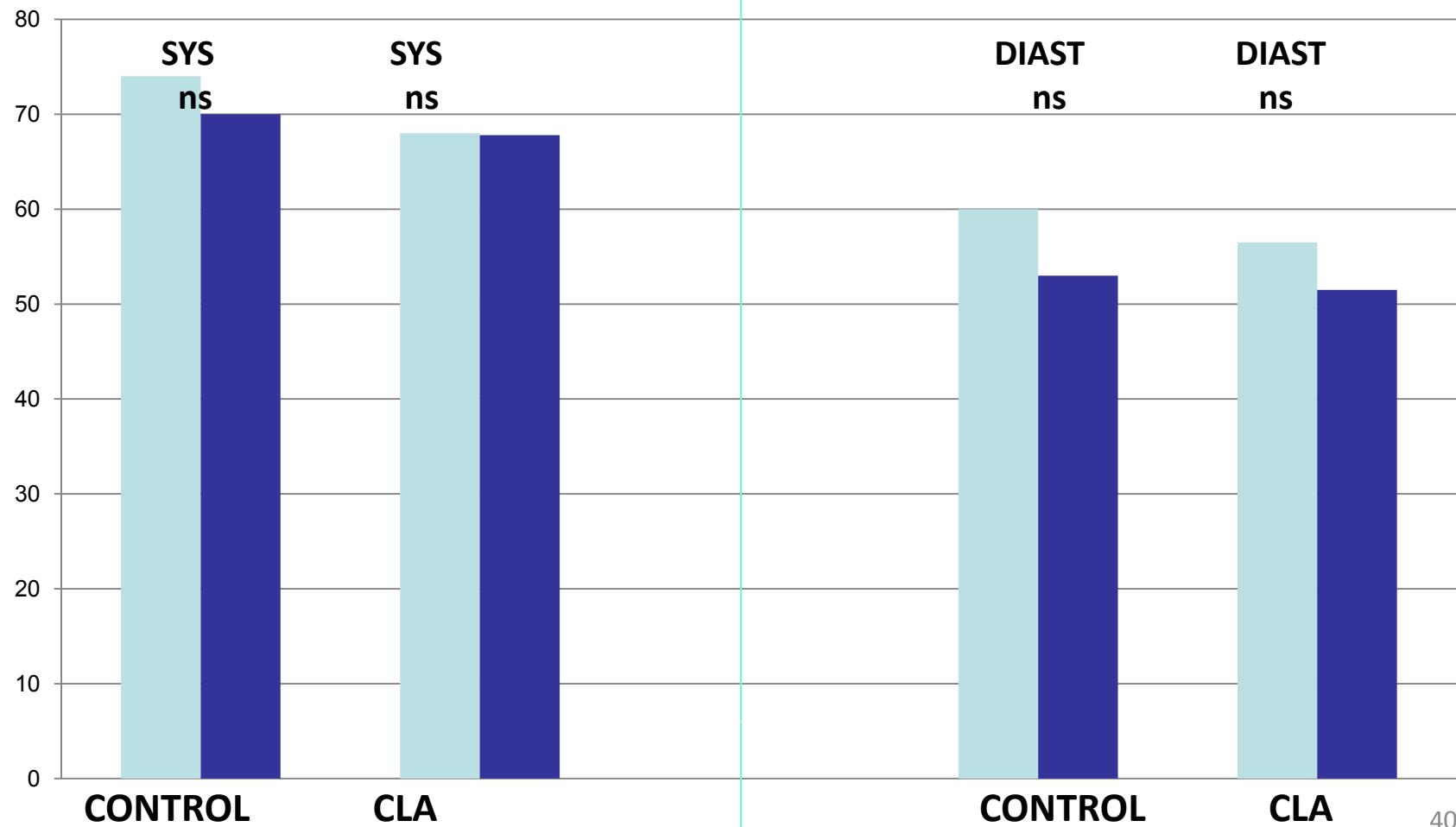
Paired T Test

BLOOD PRESSURE (Torr) VALUES AFTER 1 YEAR



CENTILE BLOOD PRESSURE VALUES AFTER 1 YEAR

Percentile for ht



THE LANCET

Volume 377, Issue 9771, 26 March 2011-1 April 2011, Pages 1085-1095

doi:10.1016/S0140-6736(11)60105-0 | How to Cite or Link Using DOI

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Articles

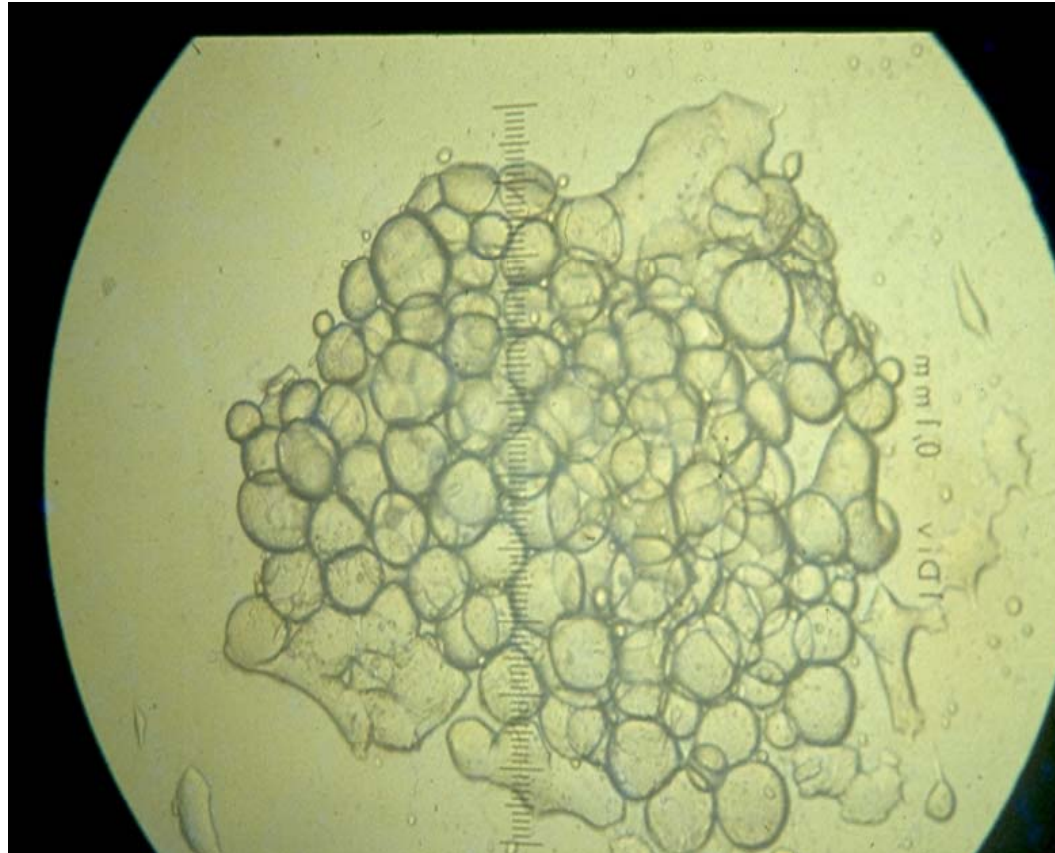
Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies

The Emerging Risk Factors Collaboration[†], , 

Av Rachel R Huxley, David R Jacobs Jr

- 221934 adults BMI > 20 kg/m², Hazard ratio 1 SD.
- BMI and Waist C. , greater risk of CVD and comorbidities

ABDOMINAL FRESH ADIPOCYTES



Moya, M. y Díaz, N.M.
"Obesidad. Aspectos histológicos actuales".
Rev. Esp. Ped. 1983; 39: 226-230.

THANK YOU



Villa Cimbrone