4º Jornadas Nacionales de Actividad Física y Deportiva en el Niño y el Adolescente

Epigenética y hábitos saludables

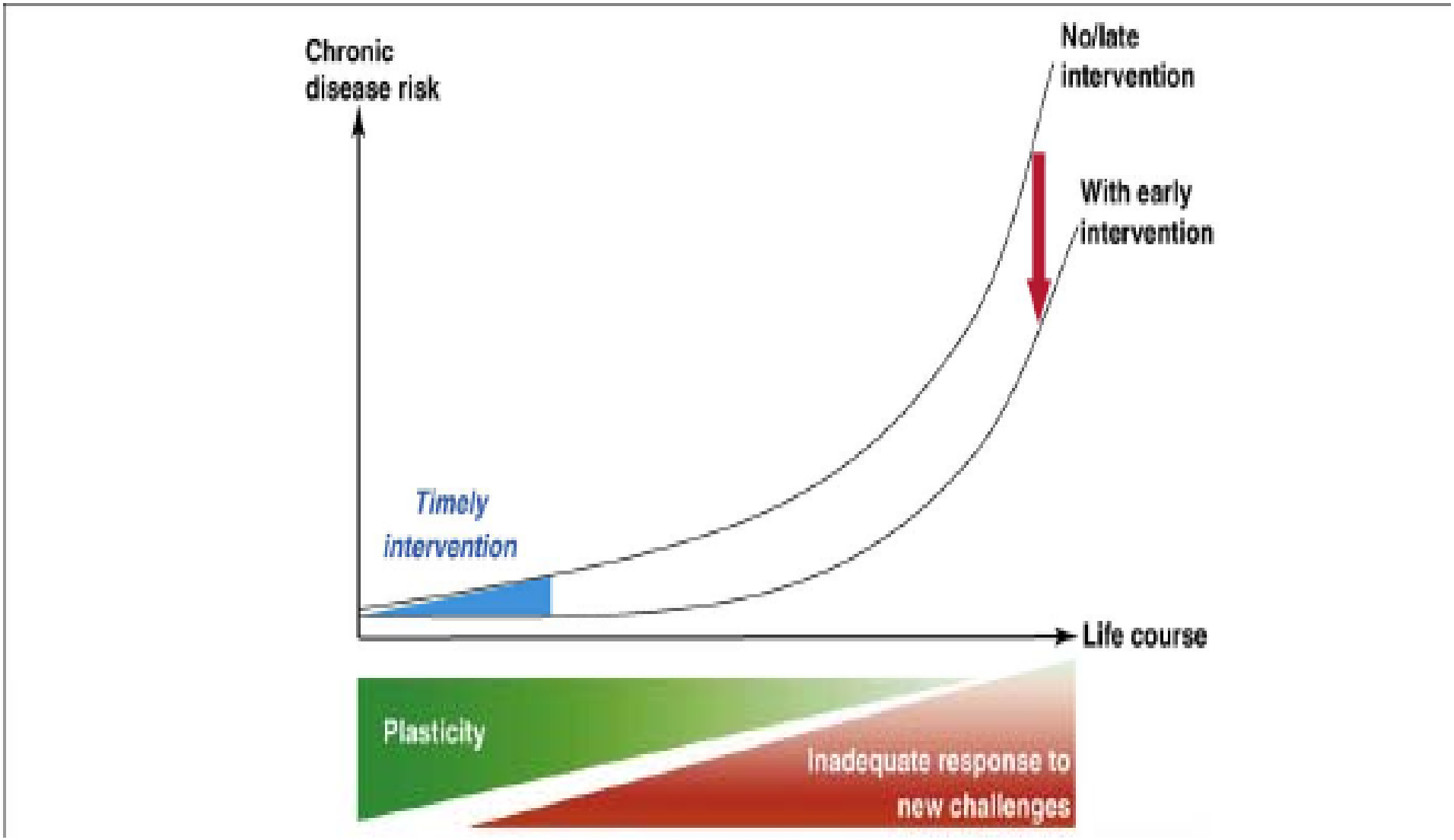
Miriam Tonietti

HNRG

- La prevalencia de obesidad y de perturbaciones metabólicas se ha incrementado dramáticamente en cada período de la vida, en la mayoría de los países del mundo.
- Más allá de la mayor disponibilidad de alimentos procesados y densamente energéticos y de la reducción en los niveles de actividad física, el ambiente energético-ambiental temprano juega un rol causal

Más del 80% de las muertes debidas a las ECNT ocurren en países en desarrollo y se espera que este número aumente en las próximas décadas . (OMS,2005)

Teoría del curso de la vida para el desarrollo de las ECNT



- Las condiciones de salud en la adultez son dependientes, en parte, de la salud nutricional de la madre y del crecimiento en la vida temprana.
- Ambos factores independientemente afectan la sensibilidad a la insulina, la composición corporal y la homeostasis energética en general

- El tamaño al nacer y el crecimiento en la infancia son reconocidos indicadores de salud en la madre y el hijo.
- En años recientes, la importancia de los patrones de crecimiento perinatales y en la niñez se han extendido.
- Hay estudios que demuestran su asociación con riesgos a muy largo plazo en la vida adulta, como la diabetes tipo 2 y la enfermedad cardiovascular

- El crecimiento es un proceso continuo
- Cualquier fenómeno que produzca una alteración temprana en la trayectoria de crecimiento puede determinar el riesgo de enfermar mucho tiempo después de ocurrida la injuria
- Fenómenos que tienen lugar en momentos posteriores en la vida pueden amplificar el riesgo de desarrollar enfermedad

DESARROLLO NORMAL

Procesos que restringen el desarrollo hacia un fenotipo particular

Variaciones en el fenotipo de acuerdo a señales ambientales tempranas

The New England
Journal of Medicine

Volume 295 AUGUST 12, 1976 Number 7

OBESITY IN YOUNG MEN AFTER FAMINE EXPOSURE IN UTERO AND EARLY INFANCY

GIAN-PAOLO RAVELLI, M.D., M.S., ZENA A. STEIN, M.A., M.B., BCH.,
AND MERVYN W. SUSSER, M.B., B.CH., F.R.C.P.

Abstract In a historical cohort study of 300,000 19-year-old men exposed to the Dutch famine of 1944-45 and examined at military induction, we tested the hypothesis that prenatal and early postnatal nutrition determines subsequent obesity. Outcomes were opposite depending on the time of exposure. During the last trimester of pregnancy and the first months of life, exposure produced significantly lower obesity rates ($P<0.005$). This result is consistent with the inference that nutritional deprivation affected a critical period of development for adipose-tissue cellularity. During the first half of pregnancy, however, exposure resulted in significantly higher obesity rates ($P<0.0909$). This observation is consistent with the inference that nutritional deprivation affected the differentiation of hypothalamic centers regulating food intake and growth, and that subsequent increased food availability produced an accumulation of excess fat in an organism growing to its predetermined maximum size. (N Engl J Med 295:349-353, 1976)

IN a historical cohort study of the Dutch famine of 1944-45, we examined prenatal and postnatal levels of nutrition as determinants of obesity in 19-year-old men. Early nutrition has been thought by some to influence adipose cell number and cell size, and in turn, adult obesity.[1,2] Others have proposed that the conditions prevailing in the prenatal period during hypothalamic differentiation can influence appetite, growth and subsequent obesity.[3] This study provides indirect tests of both hypotheses.

During the last six months of World War II, from October, 1944, until liberation, on May 7, 1945, an acute famine affected the western Netherlands. The Allied Forces had freed the Netherlands south of the Rhine, but in the west, which was still under Nazi occupation, an embargo was placed on all incoming transport, including food supplies. The embargo was a reprisal for a general strike by the Dutch railroad workers, who had responded to an appeal by the Dutch government-in-exile in London for support of the Allied Forces. Food supplies were already short, and the embargo, worsened by an unusually early and hard winter, soon resulted in famine. The famine was particularly severe in the large cities.

Available indexes of famine include the records of official food rations, measures of fetal growth, and subsequent infant mortality and general cause-specific mortality. A full description of the famine and its effects and of the data on which this study is based is given by Stein and her associates.[4] According to this account:

> At the beginning of the occupation the average daily ration for anyone not falling into a special category was about 1,800 calories. Rations were maintained at the same level in all three regions (West, North and South) until September 1944. By that time, the average daily ration had fallen to about 1,400 calories. With the onset of the famine in the West, rations were down to 1,200 calories in November, and by the turn of the year to less than 800 calories. Toward the end of February 1945, the food ration had dropped to 580 calories. Between February and April 1945, bread and potatoes formed almost the entire ration. Rations elsewhere were lower than in previous years of the occupation, but did not reach the low levels of the West. In the North, the average daily ration varied between 1,350 and 1,400 calories, and in the South between 1,375 and 1,700 calories...Supplements were given to pregnant women, mothers with young infants and the sick. During the famine however the SHAEF (Supreme Headquarters of the Allied Expeditionary Forces Report) states that "it was not always possible actually to provide these rations." Referring to conditions in The Hague the SHAEF team reports: "In the middle of November 1944 the additional supplies for mothers who were feeding their babies stopped...the allowances for pregnant women were not met."

Famine exposure in the third trimester of gestation sharply reduced post-partum maternal weight, retarded fetal growth and was followed by an excess of infant deaths in the first three months of life. Famine exposure in the first trimester of gestation, combined with some other unknown factor, was followed by an excess of premature deliveries; infants of very low birth weight, perinatal deaths and malformations of the central nervous system. Deaths during the famine, attributed to malnutrition as the primary cause and taking no account of deaths in which malnutrition was a contributing factor, numbered about 10,000.[4] Table 1 shows the average daily caloric ration in three-month averages for each region of the country.

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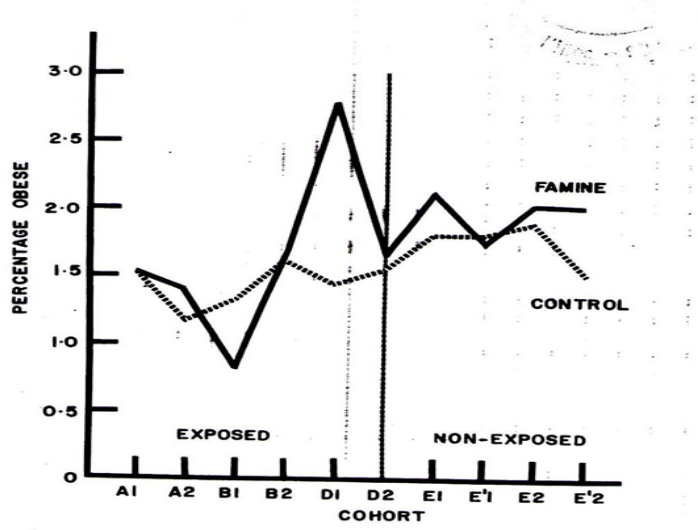
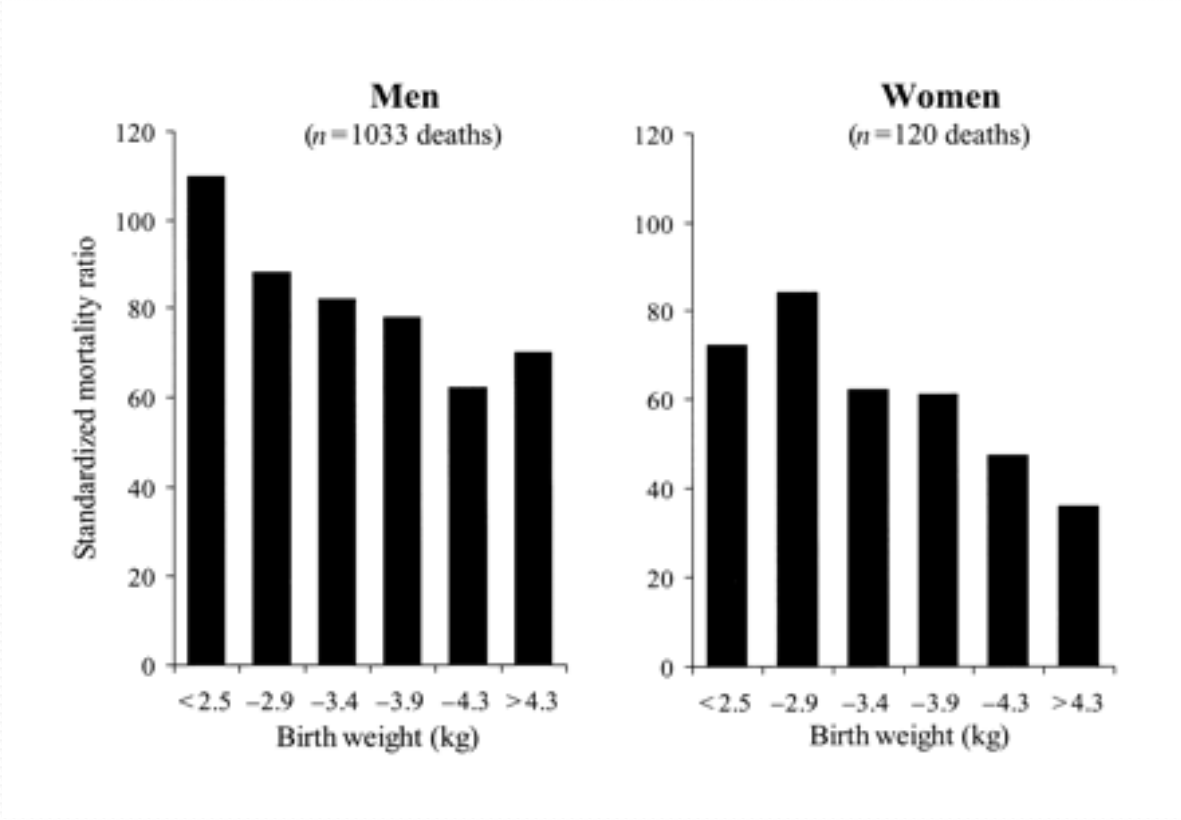


Figure 2. Obesity Prevalence Rates among Birth Cohorts in Famine and Control Areas.

Tasas de mortalidad coronaria según PN. Hertfordshire

BMJ 1993. Osmond y col



IGT y diabetes hombres a los 64 años

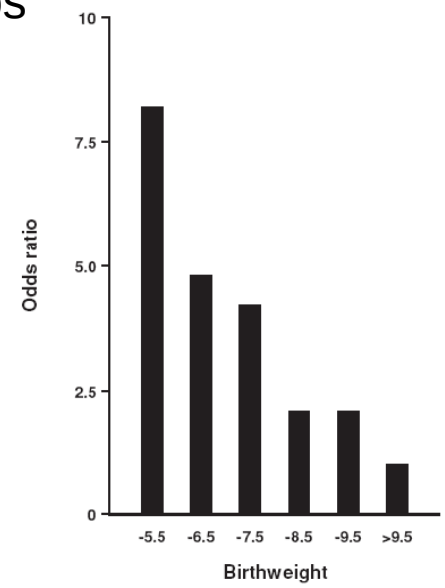


Fig. 1 Odds ratio for impaired glucose tolerance or type 2 diabetes according to birth weight among 370 men aged 64 years born in Hertfordshire (adjusted for adult body mass index).

Síndrome metabólico

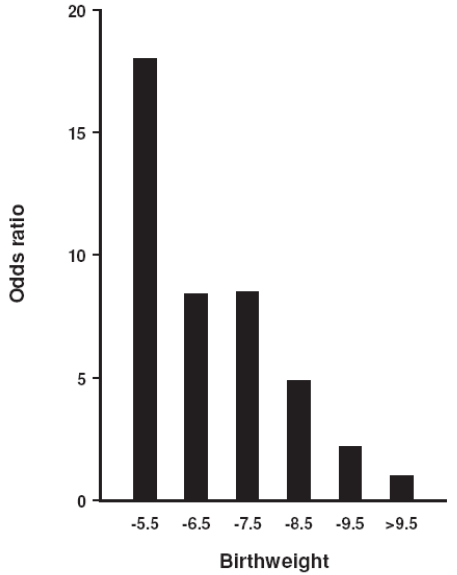
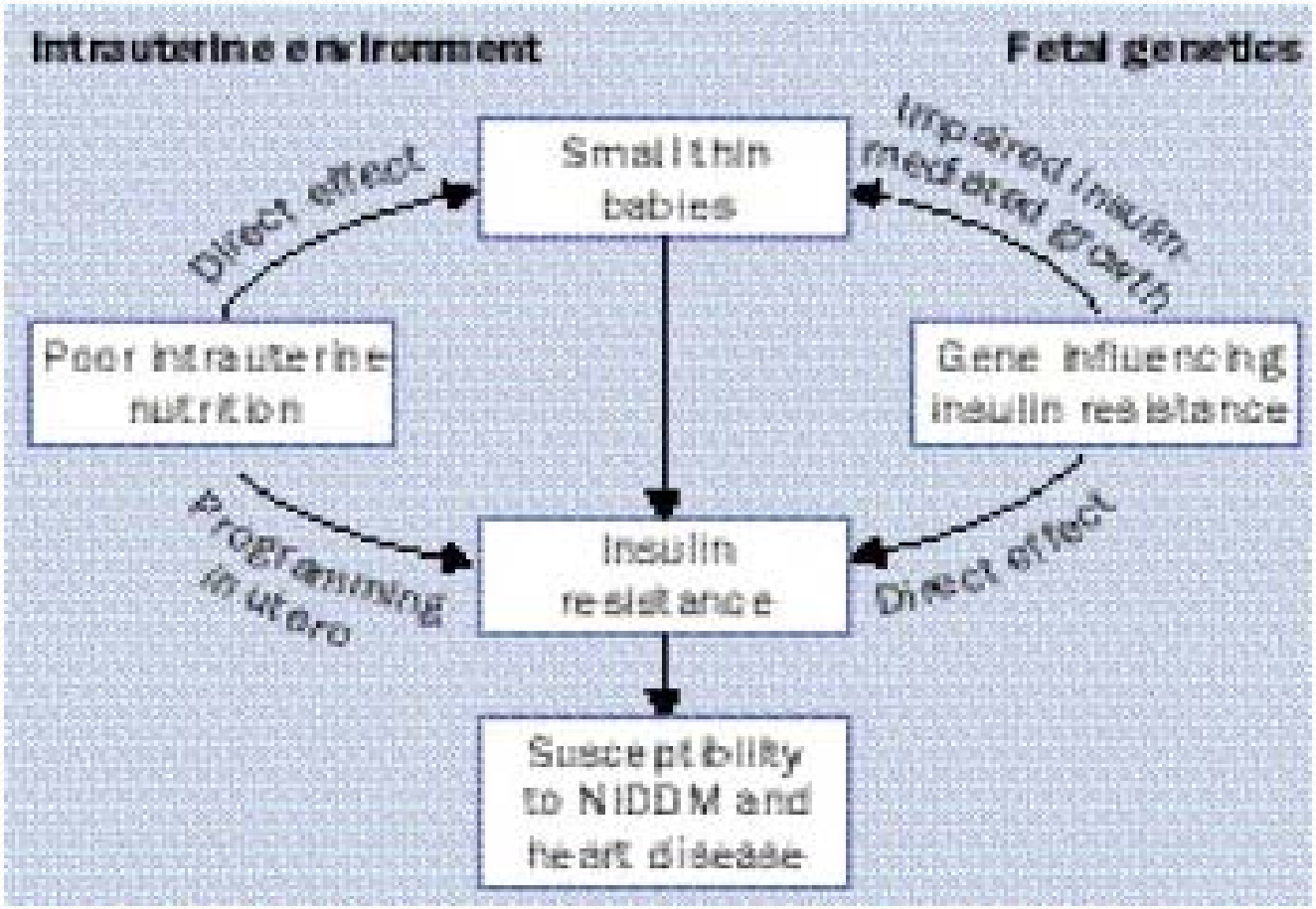


Fig. 2 Odds ratio for the metabolic syndrome according to birth weight among 407 men born in Hertfordshire (adjusted for adult body mass index).

Dos hipótesis alternativas para la asociación entre pequeño al nacer e IR, NIDDM y Enfermedad Coronaria (genes y ambiente intrauterino)



Diabetes Mellitus: A "Thrifty" Genotype Rendered Detrimental by "Progress"?

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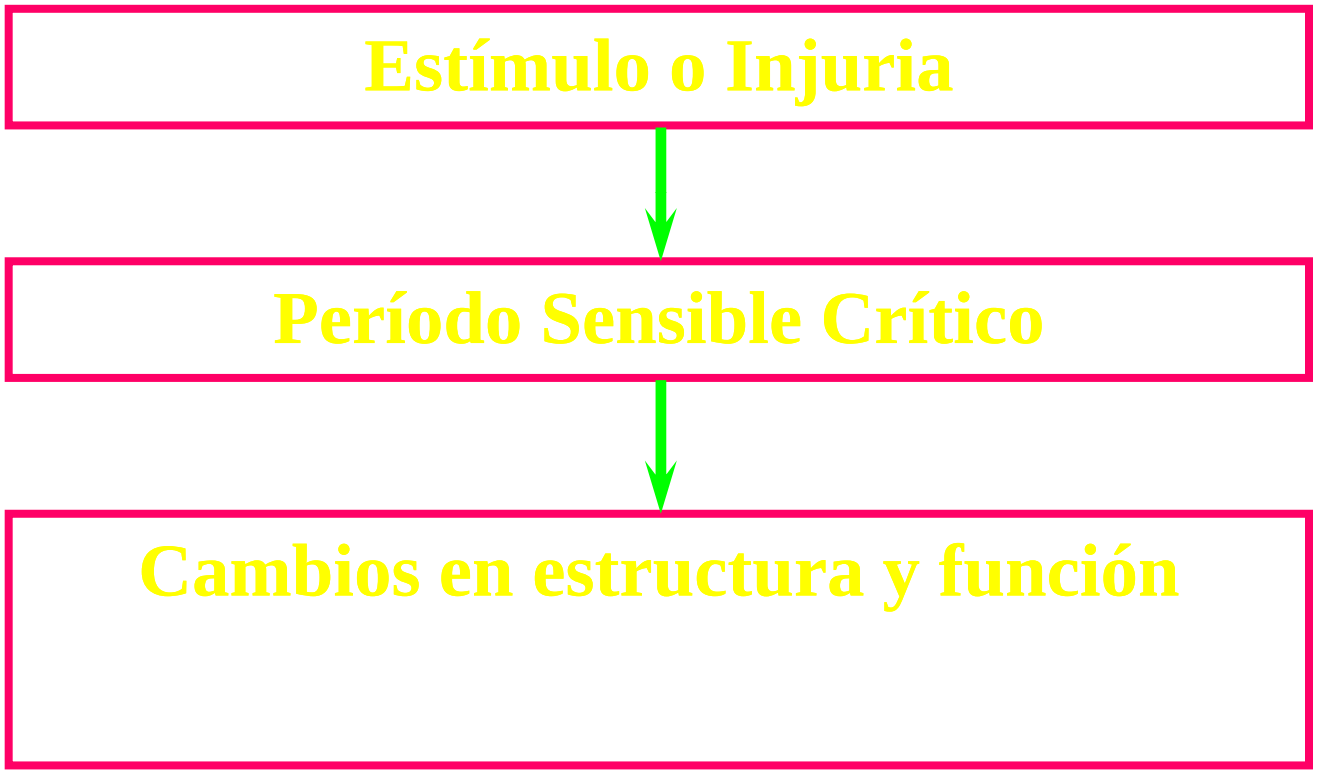
FOR THE POPULATION GENETICIST, diabetes mellitus has long presented an enigma. Here is a relatively frequent disease, often interfering with reproduction by virtue of an onset during the reproductive or even pre-reproductive years, with a well-defined genetic basis, perhaps as simple in many families as a single recessive or incompletely recessive gene (cf. Allan, 1933; Pincus and White, 1933, 1934; Harris, 1950; Steinberg and Wilder, 1952; Lamy, Frézal and de Grouchy, 1957; Steinberg, 1959; Post, 1962a). If the considerable frequency of the disease is of relatively long duration in the history of our species, how can this be accounted for in the face of the obvious and strong genetic selection against the condition? If, on the other hand, this frequency is a relatively recent phenomenon, what changes in the environment are responsible for the increase? Current developments in the study of this disease suggest an explanation with important biological ramifications.

Programming



Hipótesis del fenotipo thrifty

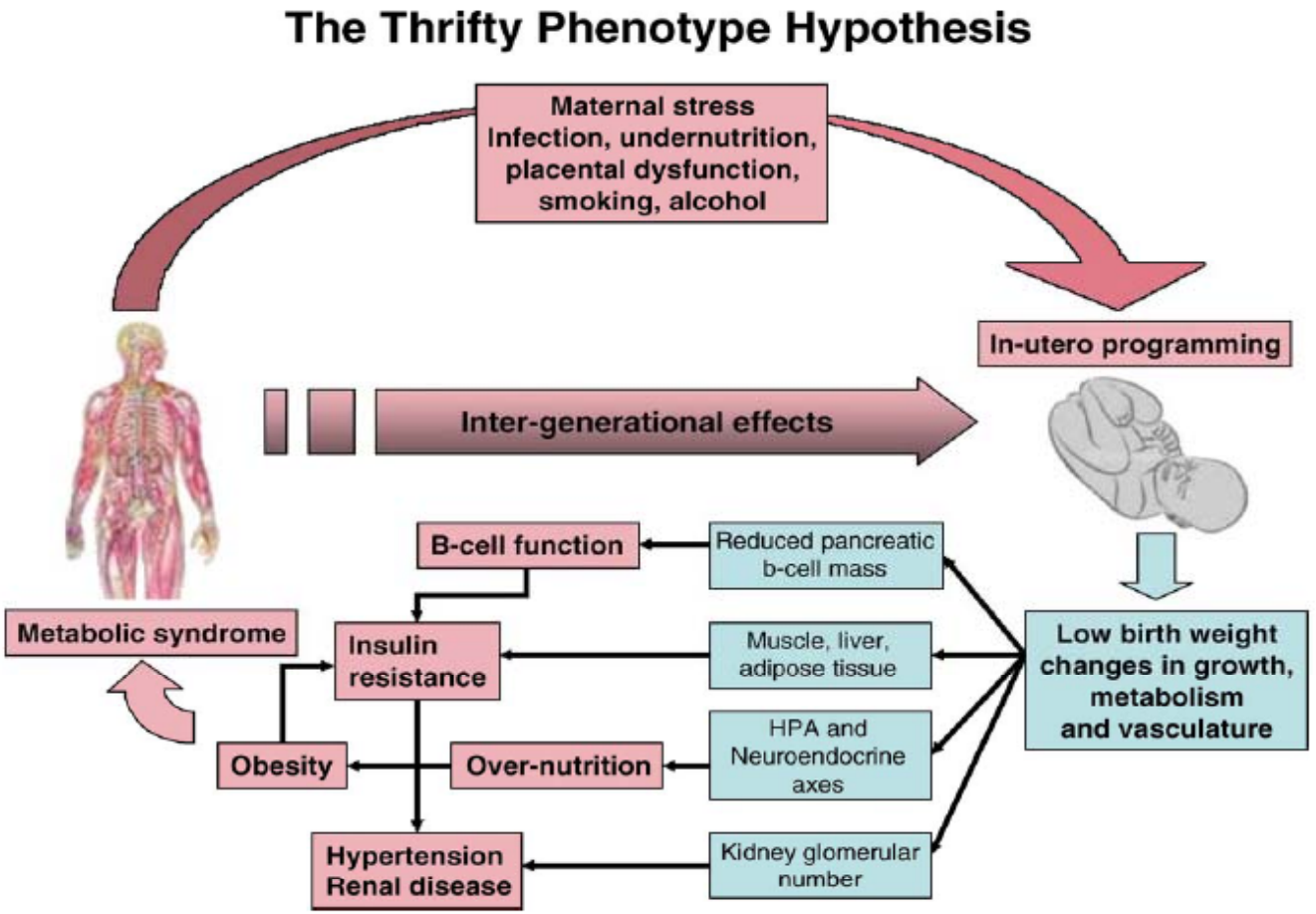
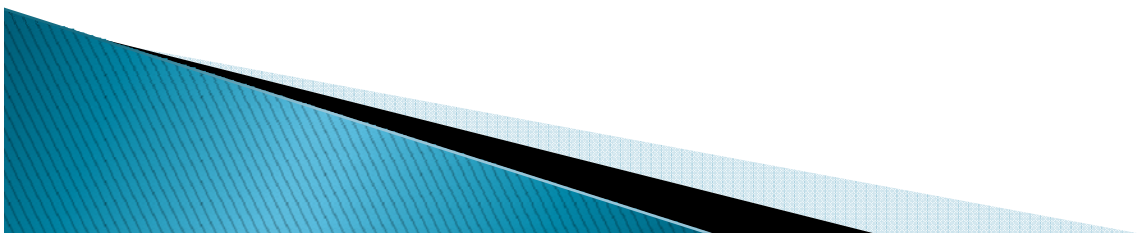


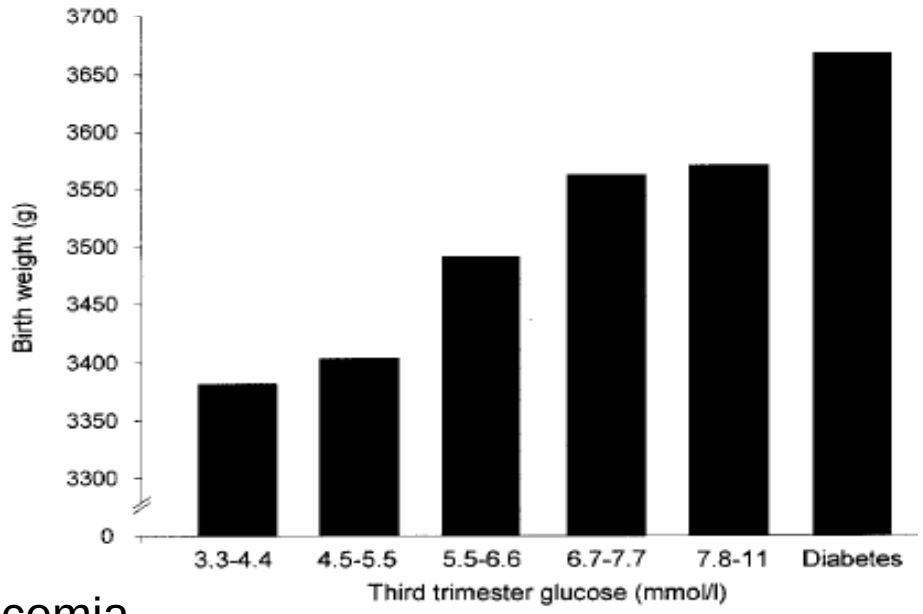
Fig. 1. A schematic representation of the Thrifty Phenotype Hypothesis, illustrating the programming effects of a suboptimal in-utero environment, nutritional or otherwise, on early growth and subsequent development of the metabolic syndrome (adapted from Hales and Barker [16]).

- El ambiente metabólico intra-uterino afecta primariamente el crecimiento del tejido adiposo y no de la masa magra..Sewell. Am J Obstet Gynecol 2006;195:110-03
- El aumento de la adiposidad en el RN se relaciona con obesidad y disfunción metabólica ya desde la infancia. Catalano PM. Am J Obstet Gynecol 2003;189: 1698-74



Asociación entre PN y glucemia materna en el tercer trimestre

Franks PW, Diabetes 2006



1SD de > glucemia materna aumento 57 g PN

Incidencia de Diabetes 2 en el RN estratificado por categoría de glucemia materna en tercer trimestre

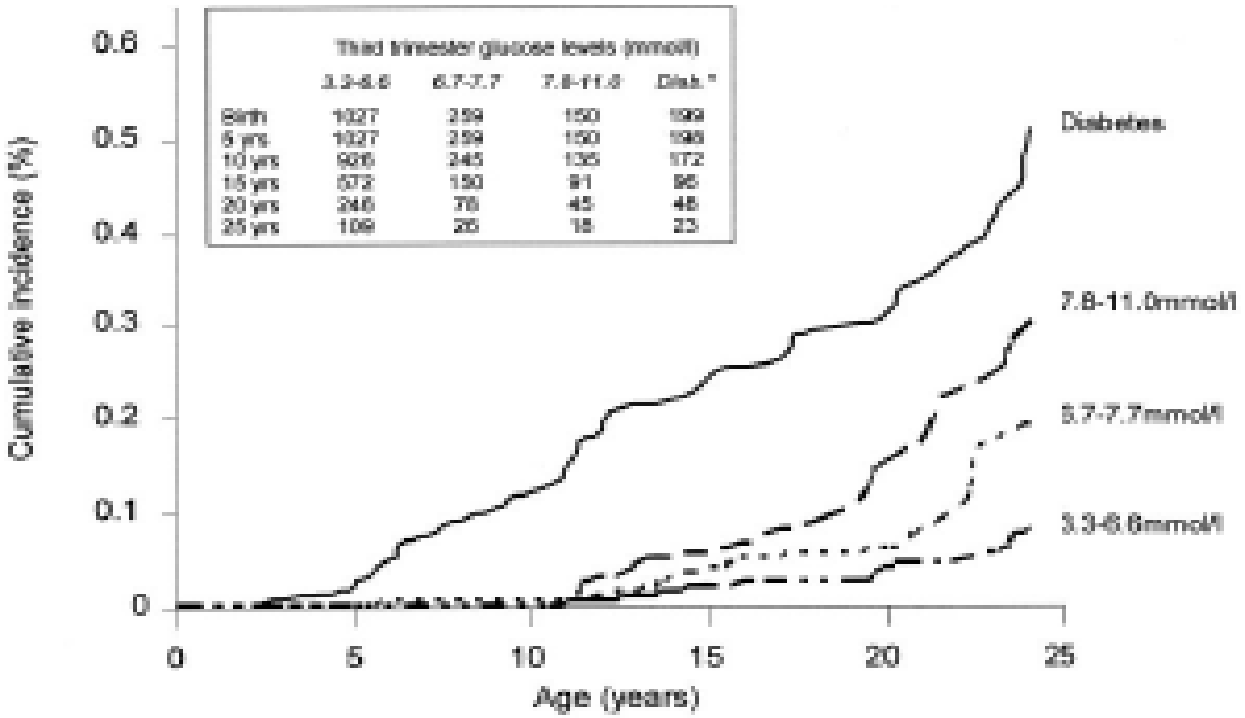


FIG. 1. Cumulative incidence of type 2 diabetes in offspring stratified by category of maternal third trimester 2-h glucose. Plots are curtailed where <10% of the original sample remains. *Insert table shows the number of individuals at risk at 5-year intervals and within third trimester glucose strata. *Type 2 diabetes in the mother diagnosed before pregnancy.

1SD de glucemia materna
aumenta 1.6 riesgo de diabetes

Franks PW, Diabetes, 2006

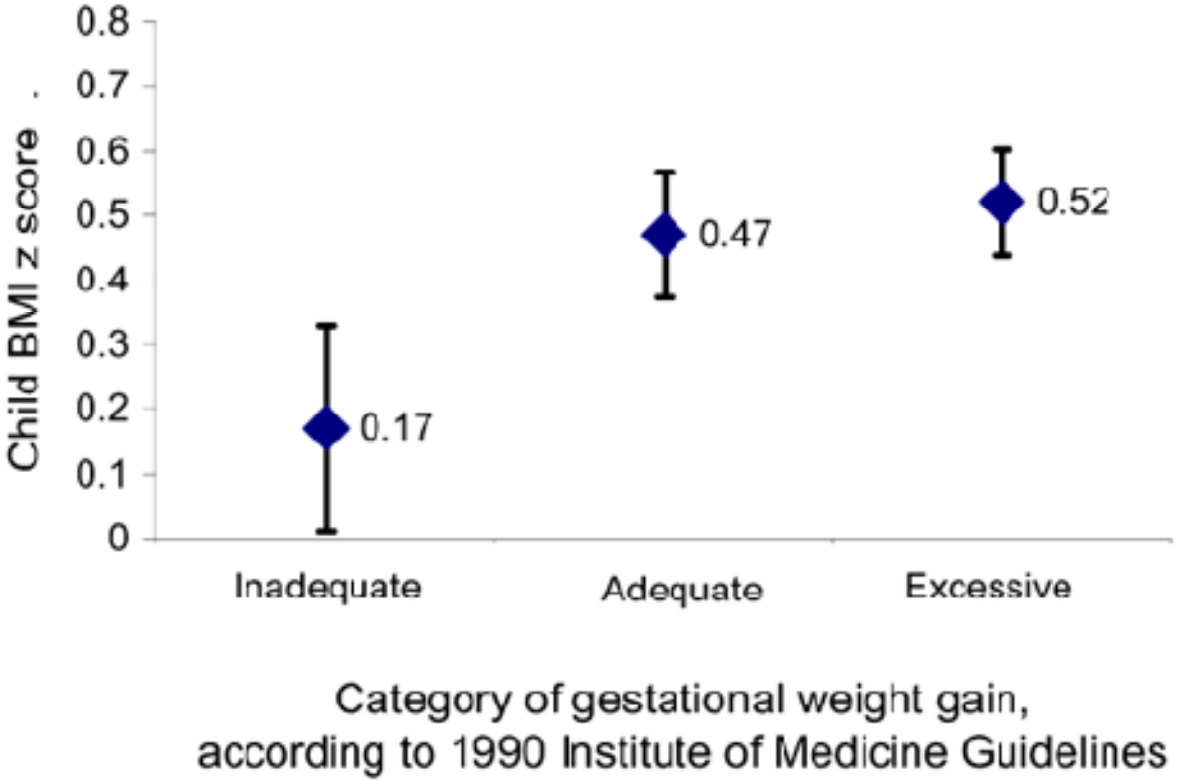
Obesidad materna y riesgo en los hijos

Table 1
A summary of studies which have reported a relationship between maternal BMI/obesity and offspring BMI/obesity or measures thereof.

Citation	Cohort size	Follow up age	Conclusion
Knight et al. 2007 [54]	547	2 years	Maternal BMI associated with offspring weight at birth, 1 year and 2 years. Maternal prepregnancy BMI is correlated with offspring BMI at 2years ($r=0.18$, $p<0.001$) during the first two years of life. After 1 year post-birth offspring BMI is also correlated with paternal BMI (at 2 years: $r=0.23$, $p<0.001$).
Whitaker et al. 2004 [123]	8494	4 years	The risk of childhood obesity at 4 years is associated with maternal obesity (measured during first trimester; BMI >30) (OR: 2.3; 95% CI: 2.0–2.6)
Burdette et al. 2006 [124]	313	5 years	Children of obese mothers (pre-pregnancy BMI >30) have 0.54 kg more fat mass than children of non-obese mothers as determined by dual-energy x-ray absorptiometry.
O'Callaghan et al. 1997 [125]	4062	5 years	Pre-pregnancy maternal obesity (≥95 percentile) (OR: 4.7; 95% CI: 3.3–6.8) and paternal obesity (≥95 percentile) (OR: 2.9; 95% CI: 1.9–4.5) are independent predictors of severe obesity (≥95 percentile) at 5 years.
Salsberry and Reagan (2005) [126]	3022	2–7 years	Maternal pre-pregnancy BMI >30 associated with an increased odds ratio for overweight in the offspring (OR: 1.37; 95% CI: 1.02–1.84)
Danzielzik et al. 2002 [74]	3306	5–7 years	Children's BMI is significantly correlated with parental BMI, although a closer correlation was observed between maternal ($r=0.249$; $p<0.01$) than paternal ($r=0.159$; $p<0.01$) BMI. Also there was a closer correlation between the BMI of boys and parental BMI than that for girls.
Blair et al. 2007 [127]	871	7 years	Maternal obesity (BMI >30) results in higher offspring body fat measured by bioelectrical impedance analysis (OR: 4.0 (95% CI: 0.4–7.7)
Fisch et al. 1975 [128]	1779	7 years	Maternal index (kg/cm) is associated with offspring obesity at 7 years of age ($p<0.5$)
Reilly et al. 2005 [129]	8234	7 years	Maternal BMI during pregnancy and Paternal BMI are independent predictors of obesity at 7 years (both parents: adjusted OR: 10.44; 95% CI: 5.11–21.32).
Davey Smith et al. 2007 [130]	4654	7.5 years	Child BMI is associated equally with maternal ($r=0.295$ (0.267 to 0.322)) and paternal ($r=0.250$ (95% CI: 0.218 to 0.274)) BMI
Gale et al. 2008 [83]	216	9 years	For 1 standard deviation increase in maternal pre-pregnancy BMI, fat mass index increased by 0.26 standard deviations.
Li et al. (2005) (131)	2636	2–14 years	Maternal pre-pregnancy BMI >30 associated with an increased odds ratio for overweight in the offspring (adjusted OR: 4.1; 95% CI): 2.6–6.4)
Lawlor et al. 2007 [132]	3340	14 years	Pre-pregnancy maternal BMI (β 0.353 (95% CI: 0.304–0.401) a stronger predictor of offspring BMI than paternal BMI (β 0.251 (95% CI: 0.199–0.304) (difference between maternal and paternal: $p=0.009$)
Koupil and Toivanen 2008 [133]	1103	18 years	Maternal pre-pregnancy BMI is the strongest predictor of offspring obesity (OR: 0.39; 95% CI: 0.28–0.49)
Parson et al. 2001 [134]	17,414	33 years	Pre-pregnancy maternal BMI explained association between birth weight and adult BMI

- Niños nacidos de madres obesas tienen 2 veces más riesgo de ser obesos a los 2 años (Whitaker 2004).
- El peso de la madre anterior a la concepción es un factor de riesgo adicional para obesidad en la adolescencia (Yogev & Langer 2008).
- Adolescentes nacidos de madres obesas o con DM tienen doble riesgo de tener sindrome metabólico (Boney et al. 2005).
- Hay una fuerte correlación entre el IMC materno y el IMC del hijo en la adultez

Gestational weight gain and child adiposity at age 3 years. Oken E, *Am J Obstet Gynecol*. 2007 ;196(4):e1–e8



Dabelea D et al. Diabetes, vol. 60, July 2011

Catch up en la niñez y muerte por enfermedad coronaria. Eriksson J et al. BMJ 1999

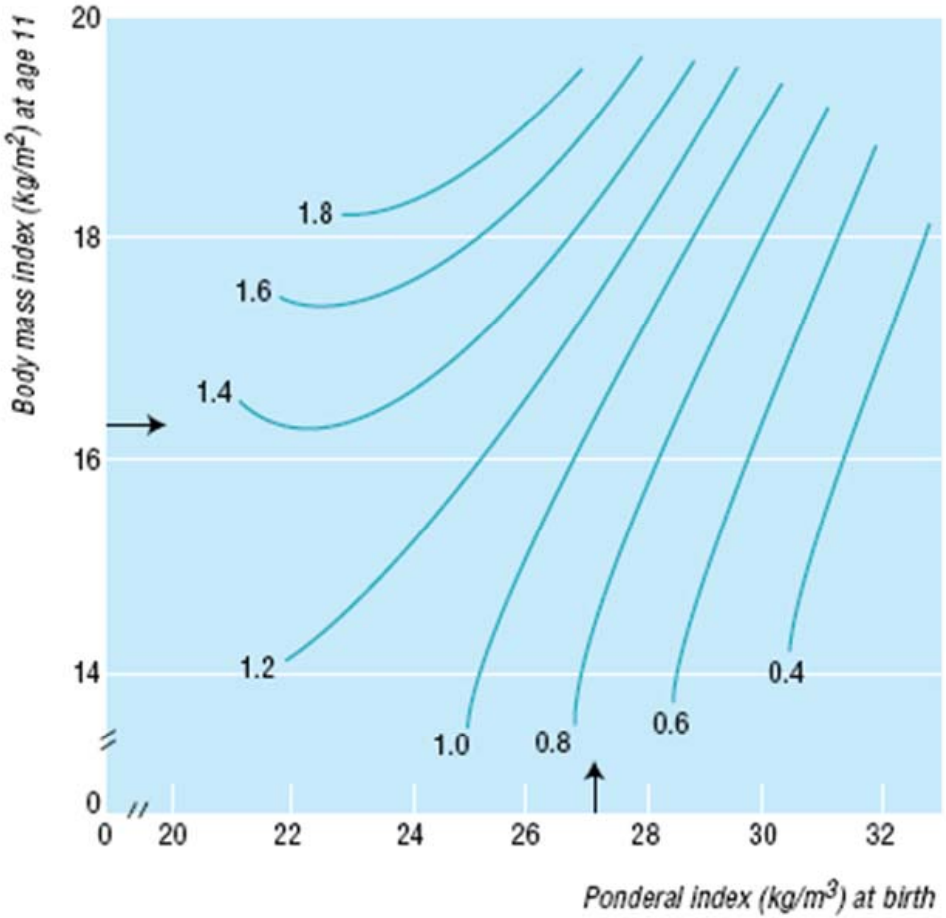


Fig 2 Hazard ratios for death from coronary heart disease according to ponderal index at birth and body mass index at age 11 years, adjusted for length of gestation. Arrows indicate average values

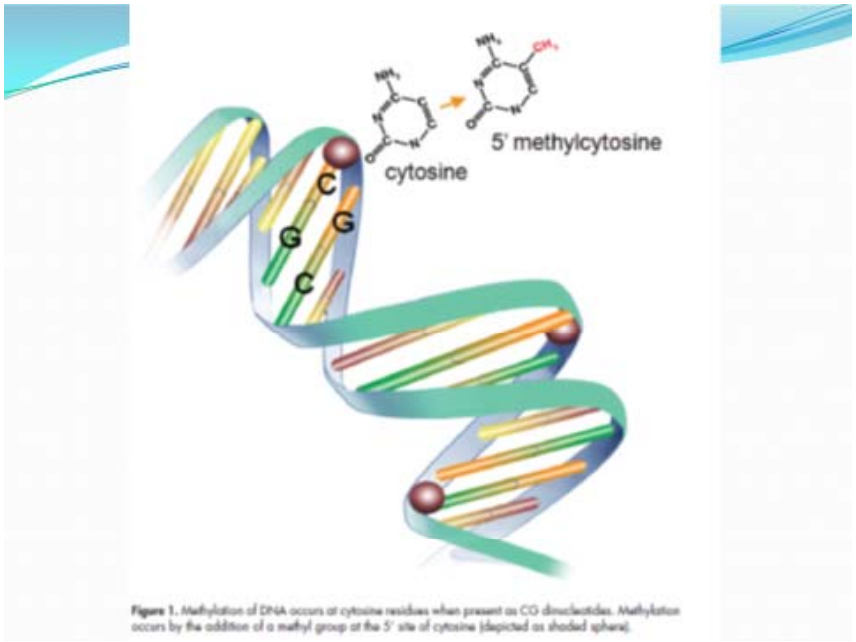
Epigenética

- Rama de la biología que estudia la relación causal entre los genes y sus productos, de los cuales emerge el fenotipo final.
- La regulación epigenética mediaría la adaptación de la expresión del genoma para generar distintos fenotipos ante las diferentes condiciones ambientales
- Modificaciones en la conformación de la cromatina sexual

(combinación del ADN con un grupo proteico, histonas) y su relación en la expresión génica

Epigenética

- 30000 genes codificantes
- Estado de cromatina: crítico para determinar cuándo, cómo y dónde se establece la transcripción de un gen en un producto determinado
- Heterocromatina: altamente condensada, impide el acceso de los elementos activadores de la transcripción y determina silenciamiento génico de la zona
- Eucromatina: más laxa, permite acoplamiento de activadores en regiones promotoras y la transcripción



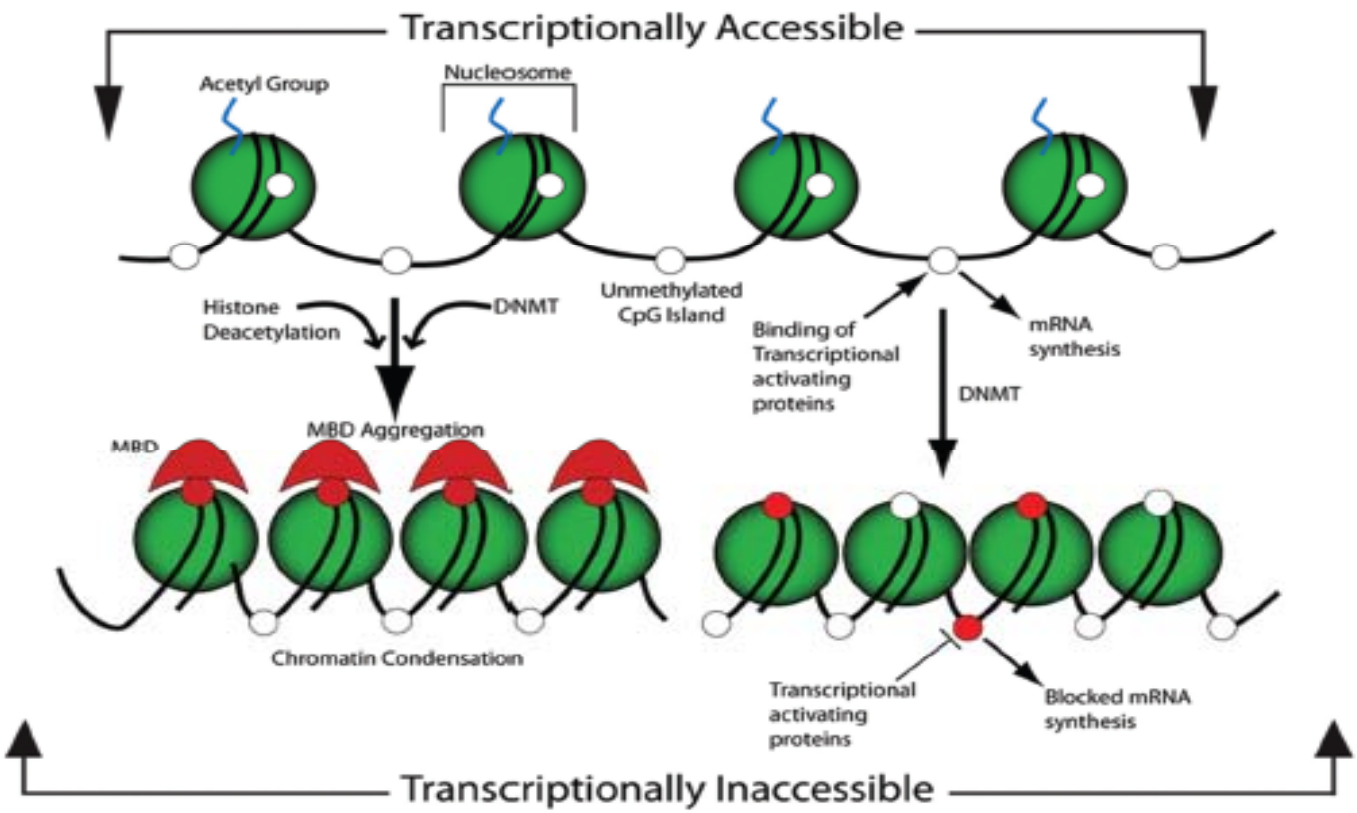


Figure 2. The shaded sphere depicts the octameric histone complex, which forms the nucleosome with the acetylated tails of histones and the cytosines of the CpG sites in an unmethylated state, shown as open white circles. In this conformation, the chromatin is loosely packed and available for the binding of transcriptional activating proteins, which, by the action of RNA polymerase II, synthesize mRNA. The action of DNA methyl transferase (DNMT) methylates the cytosine residues, depicted as red circles, which provide a docking site for the methyl binding domain proteins (MBD), which aggregate in conjunction with the action of the histone deacetylase, which cleaves the histone acetyl group. Both of these serve to alter the structure of the chromatin by causing a condensation that impedes the access of the transcriptional activating proteins and thereby blocks mRNA synthesis. Alternatively, the normal active structure of chromatin can become inaccessible for the binding of transcriptional activating proteins by the action of CpG methylation at sites that sterically hinder the binding of activating proteins, independent of MBD aggregation.

Programación epigenética por factores nutricionales tempranos

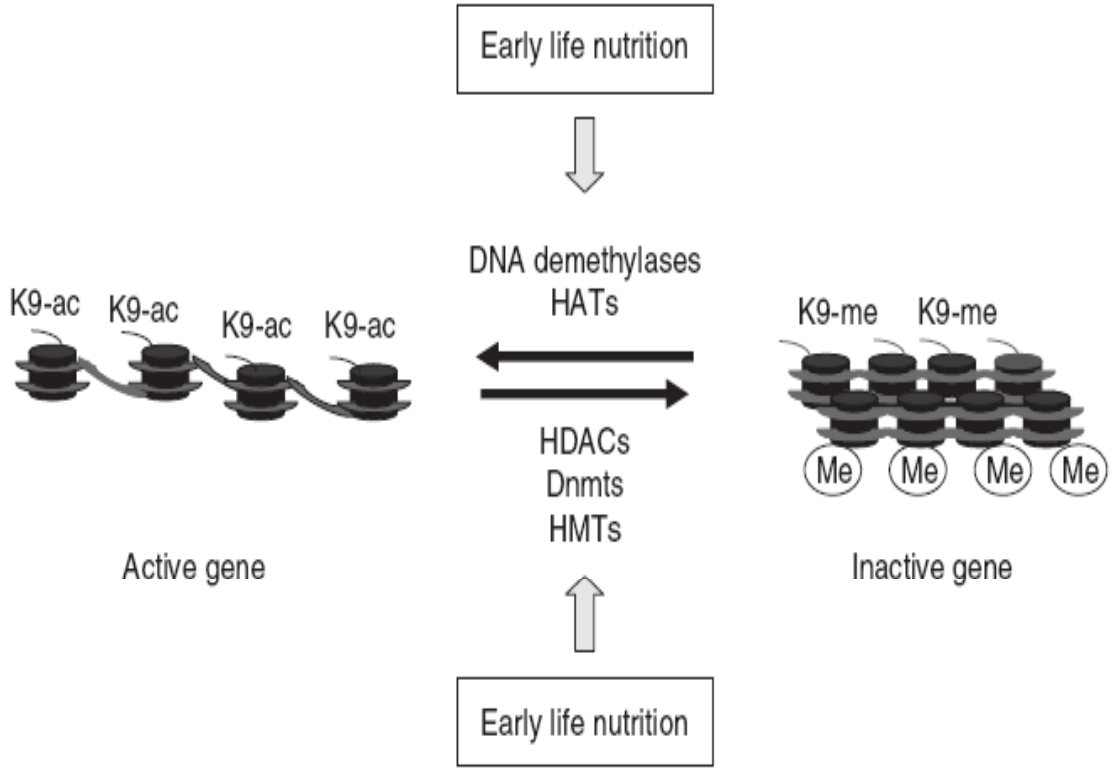


Figure 2 Epigenetic programming by early-life nutrition. Nutrition in early life determines the balance between gene methylation and demethylation. HDACs, HMTs and Dnmts promote histone deactylation, histone K9 and DNA methylation, resulting in a closed chromatin structure and gene silencing. Histone acetyl transferases (HATs) and DNA demethylases induce histone acetylation and DNA demethylation resulting in an open chromatin structure and gene transcription.

Plasticidad del desarrollo

- Fenómeno por el cual un genotipo puede dar lugar a una variedad de diversos estados fisiológicos y morfológicos (fenotipo) en respuesta a diferentes condiciones ambientales durante el desarrollo.
- Desde el punto de vista evolutivo tiene ventajas ya que permite la conformación fenotípica que mejor se adapta al medio ambiente en el que le toca desarrollarse

- La ventaja adaptativa de tales respuestas está determinada por la probabilidad que las elecciones hechas durante el desarrollo temprano son apropiadas para enfrentar el ambiente en el que el organismo se desarrollará durante su maduración y vida reproductiva.
- Si la predicción coincide con el ambiente posterior, ese organismo adaptará perfectamente y asegurará una selección positiva.

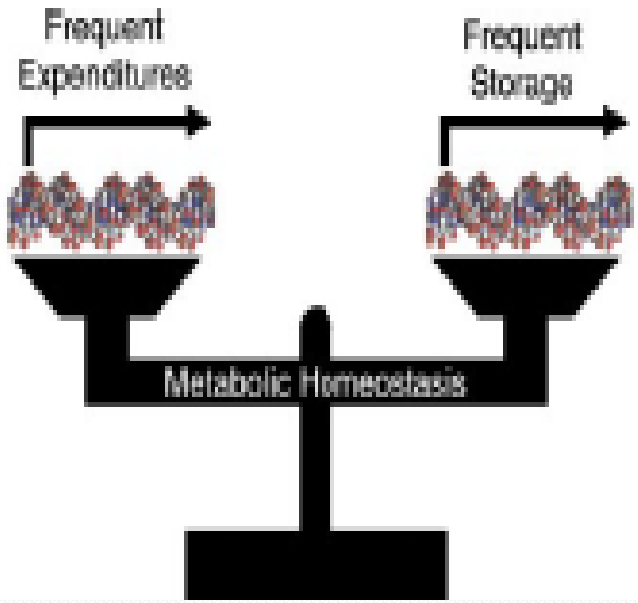
¿CÓMO LLEGAMOS A SER LO QUE SOMOS?

- Potencial genético
- Medio ambiente:Nutrición

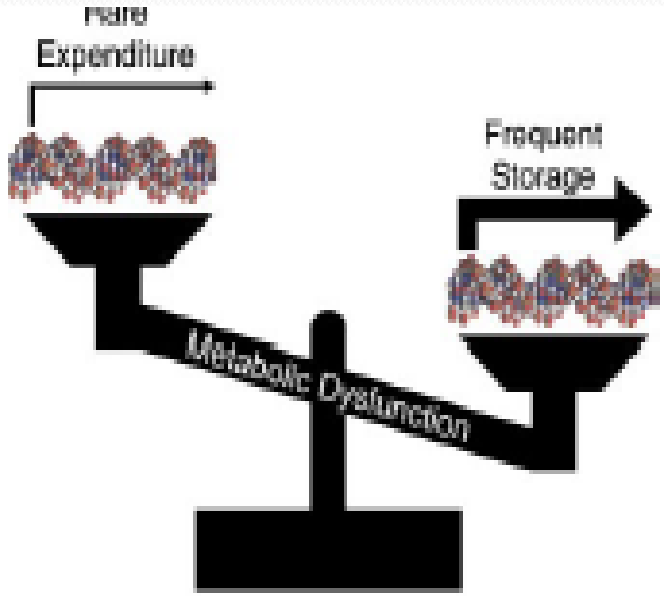
  Estilo de vida

  Factores socioeconómicos

Balance adecuado AF/Inactividad permite expresión balanceada de genes de almacenamiento y gasto de energía



Disminución AF promueve balance maladaptativo en expresión de genes de almacenamiento y gasto



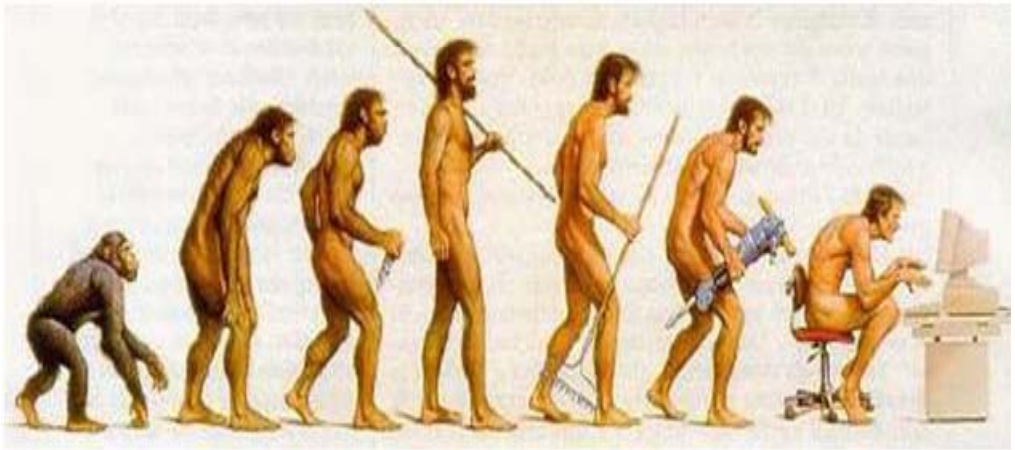
Una de las causas primarias del desarrollo de ECNT, todavía subapreciada, es la falta de actividad física diaria suficiente: la INACTIVIDAD FÍSICA

El genoma humano permaneció sin grandes cambios durante los últimos 10000 años

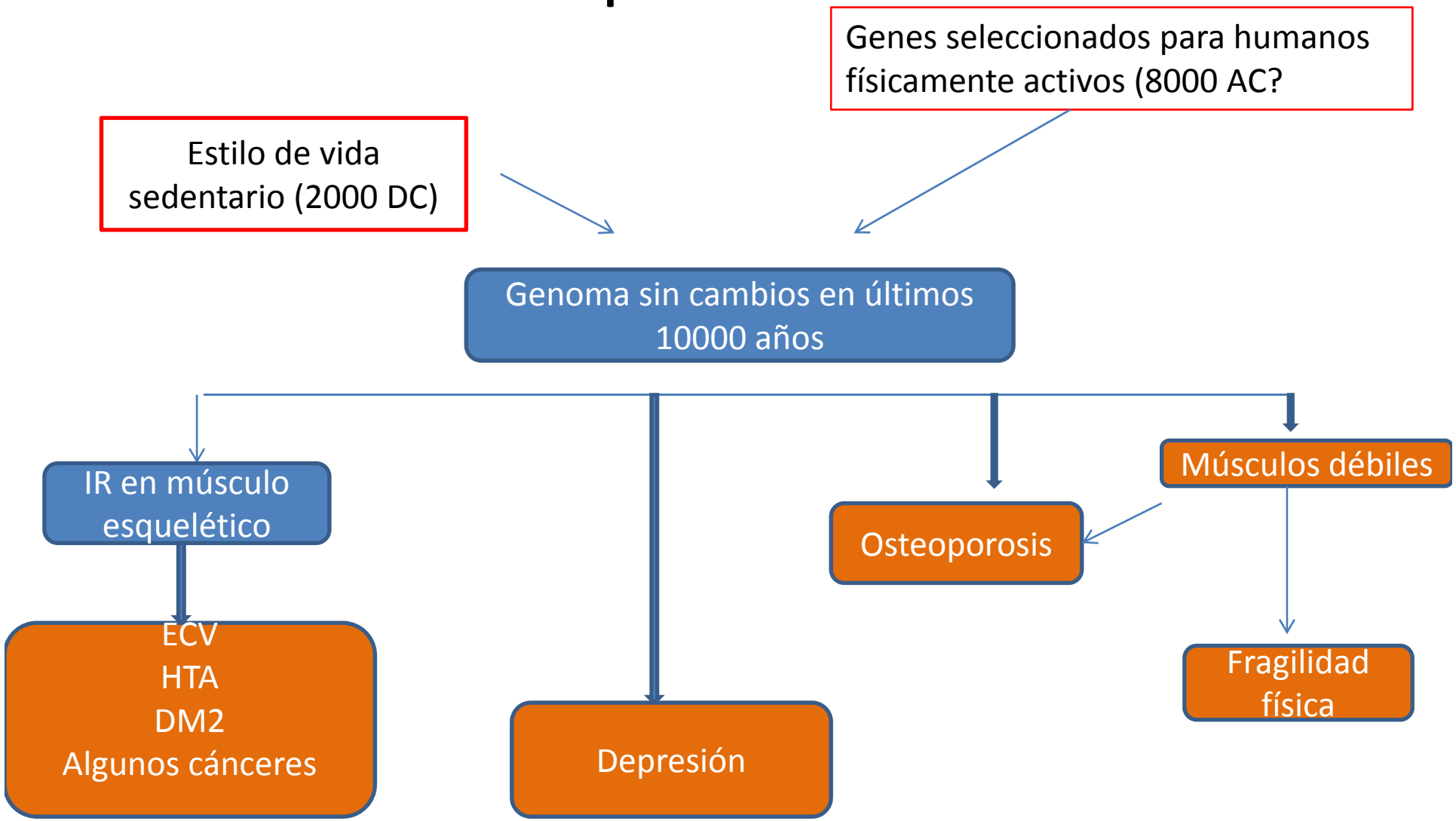
El genoma humano evolucionó para tolerar altas tasas metabólicas y actividades de fuerza en un estilo de vida físicamente activo

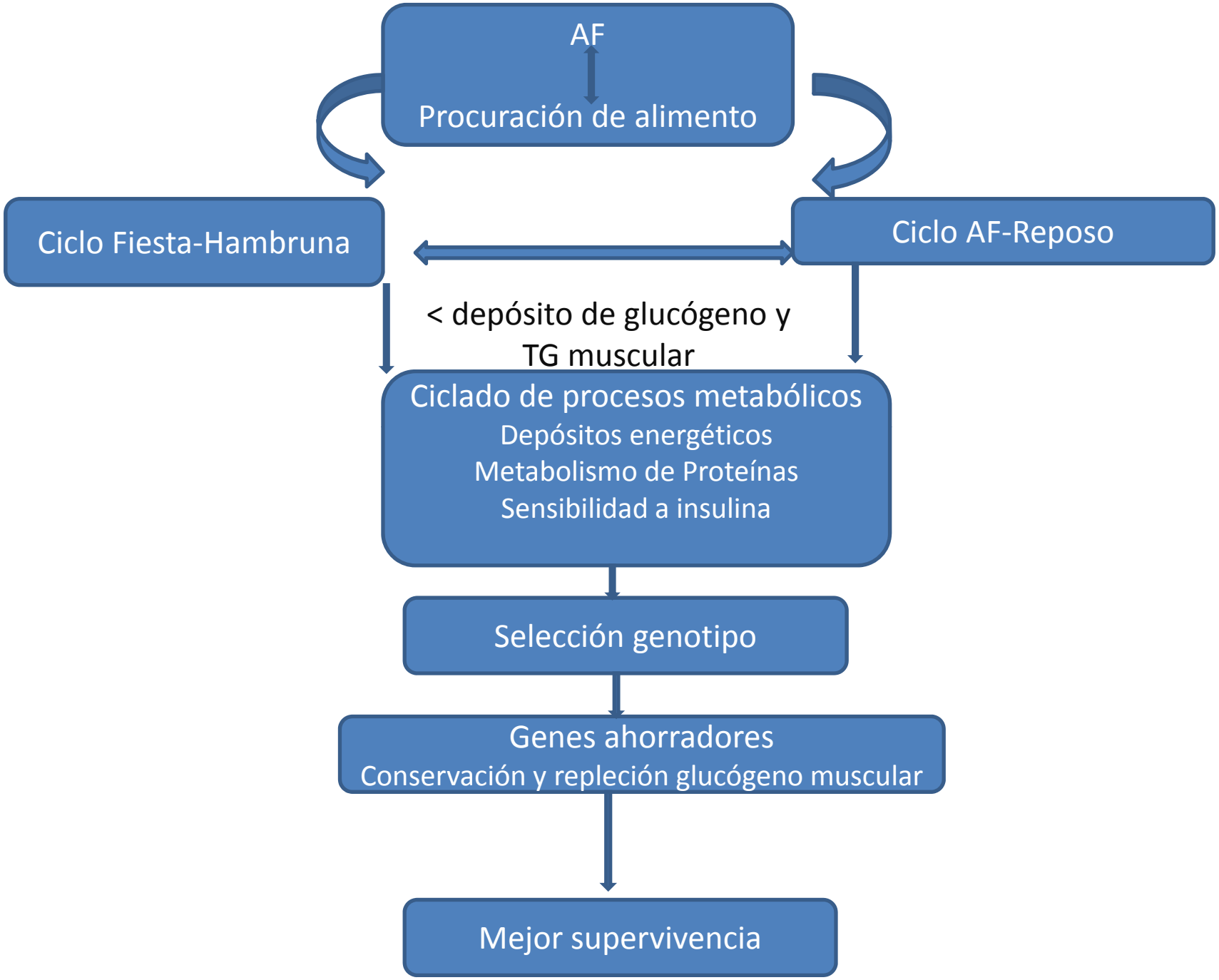
- El estilo de vida actual físicamente inactivo no mantiene los flujos metabólicos y de carga muscular requeridos para el normal funcionamiento de nuestros “viejos” genes

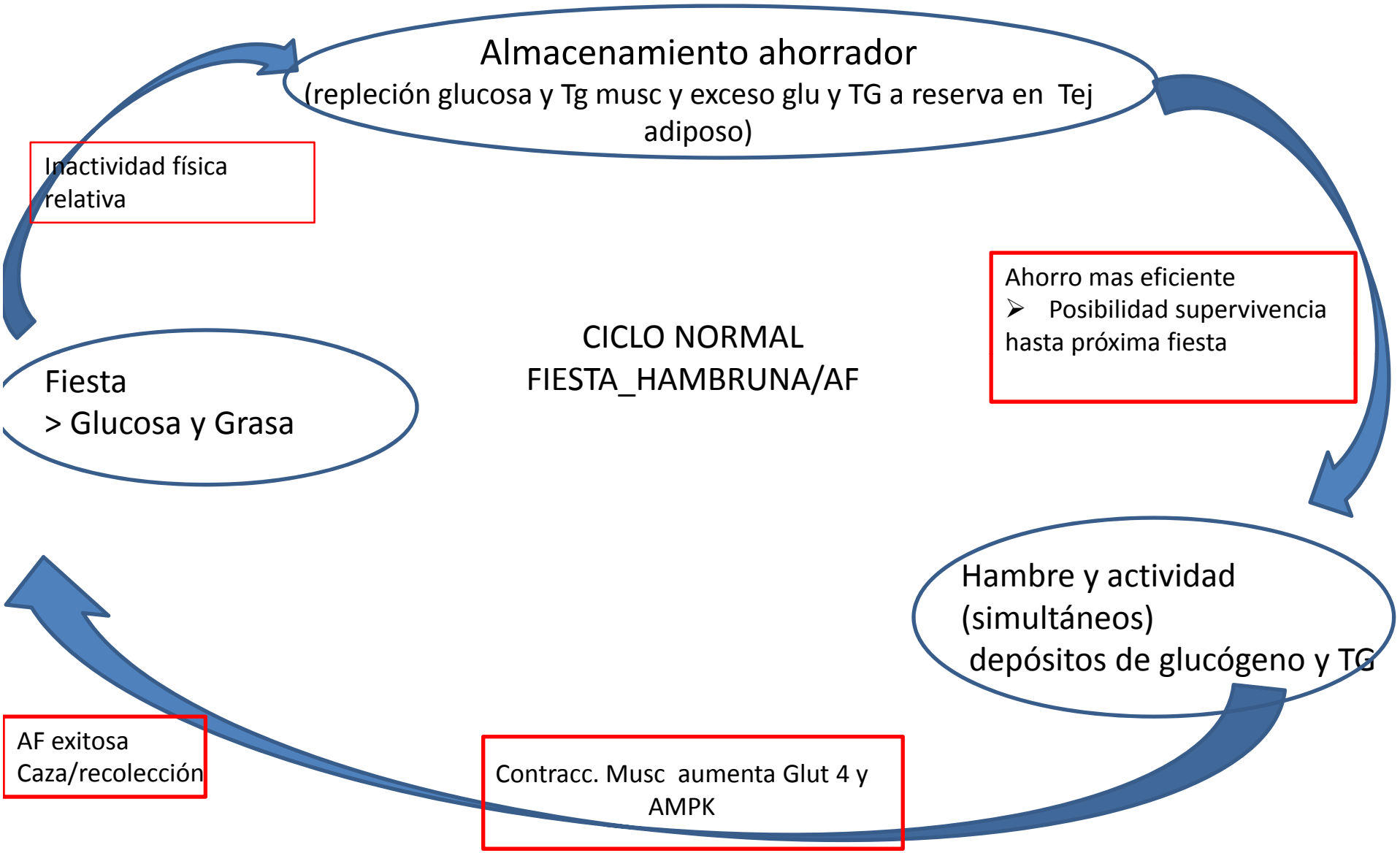
Los genes que esperan de la actividad física para funcionar adecuadamente alteran su expresión y resultan en un fenotipo con alteraciones clínicas manifiestas



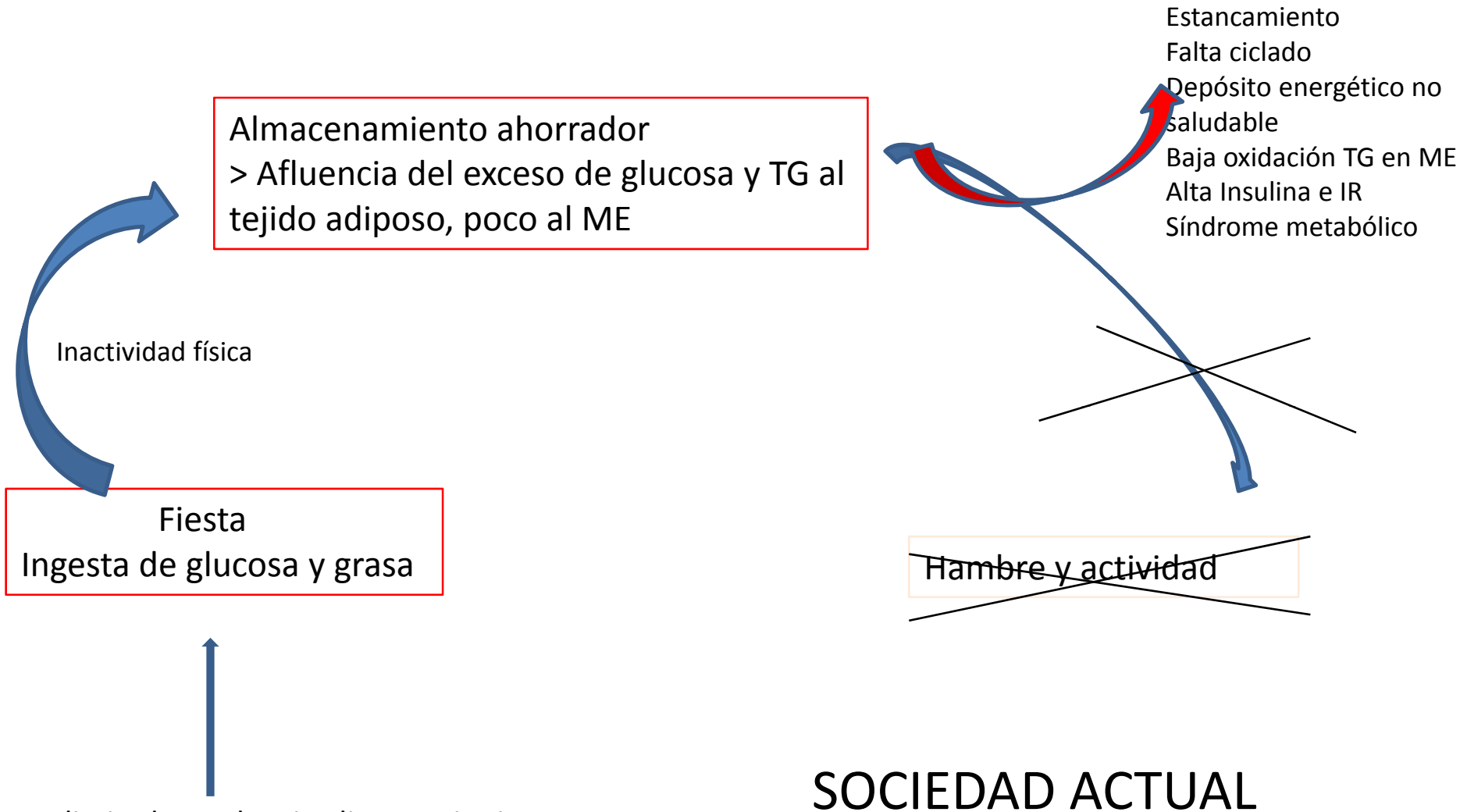
Nuestros genes necesitan de la actividad física para mantener la salud



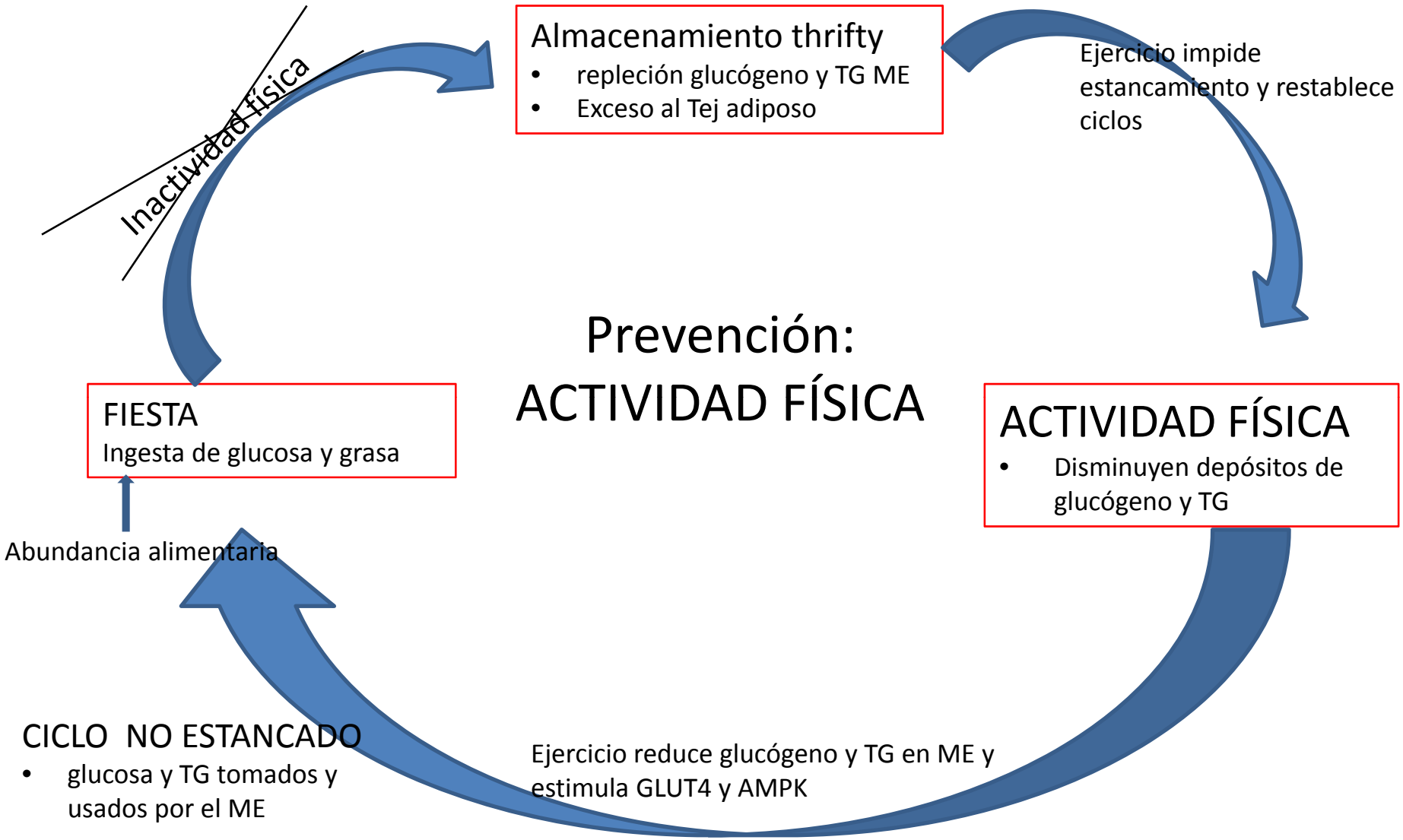

AF
Procuración de alimento
Ciclo Fiesta-Hambruna
Ciclo AF-Reposo
< depósito de glucógeno y
TG muscular
Ciclado de procesos metabólicos
Depósitos energéticos
Metabolismo de Proteínas
Sensibilidad a insulina
Selección genotipo
Genes ahorradores
Conservación y repleción glucógeno muscular
Mejor supervivencia



Modificado de J Appl Physiol vol 96, 2004



SOCIEDAD ACTUAL


Inactividad física
Almacenamiento thrifty
• repleción glucógeno y TG ME
• Exceso al Tej adiposo
Ejercicio impide estancamiento y restablece ciclos
Prevención:
ACTIVIDAD FÍSICA
ACTIVIDAD FÍSICA
• Disminuyen depósitos de glucógeno y TG
FIESTA
Ingesta de glucosa y grasa
Abundancia alimentaria
CICLO NO ESTANCADO
• glucosa y TG tomados y usados por el ME
Ejercicio reduce glucógeno y TG en ME y estimula GLUT4 y AMPK

Ejercicio e IR

- El transportador GLUT 4 aumenta en la membrana de la célula músculo liso INDEPENDIENTEMENTE de la insulina
- La insulina y el ejercicio reclutan GLUT4 desde 2 sitios diferentes de depósito intracelular muscular
- La translocación de GLUT4 mediada por insulina en músculo requiere del uso de muchas proteínas que no están comprometidas en la translocación del GLUT4 durante el ejercicio

- La IS aumenta post ejercicio SIN utilizar el receptor de insulina ni el IRS (aparentemente regulada por combinación de factores séricos, mecanismos auto y paracrinos, y concentración del glucógeno muscular)

La INACTIVIDAD FÍSICA produce IR en músculo esquelético en cuestión de horas

Efectos de la inactividad

- Modelo: reposo en cama
- Reducción de la IS y alteración de la expresión de más de 4500 genes
- Supresión de 54% de genes implicados en la biogénesis mitocondrial (algunos de ellos suprimidos en DM2)
- Se normalizan parcialmente después de 4 semanas de reentrenamiento

Am J Physiol Endocrinol Metab 2010; 299:E752–E763.

Correr es una conducta intrínseca que apareció con el género Homo hace aproximadamente 2.000.000 de años y que probablemente determinó las adaptaciones estructurales que contribuyeron al éxito final del Homo sapiens como especie

Cambios direccionales en procesos regulatorios metabólicos

	FIESTA	RECUPERACION EJERCICIO	HAMBRUNA	EJERCICIO
GLUCEMIA	↑↓	↑ (SI < cn Ex)	↓	↓
INSULINEMIA	↑	↑ (de nivel bajocnEx)	↓	↓
IS	↓	↑	↓	↑
NIVEL GLUCOGENO ME	↑	↑ (de nivel bajo cn Ex)	↓	↓
OXIDACION AG ME	↓	↓ (de nivel alto cn Ex)	↑	↑ (aumenta para preservar glúcógeno musc)

Promedio diario de ingesta de Energía

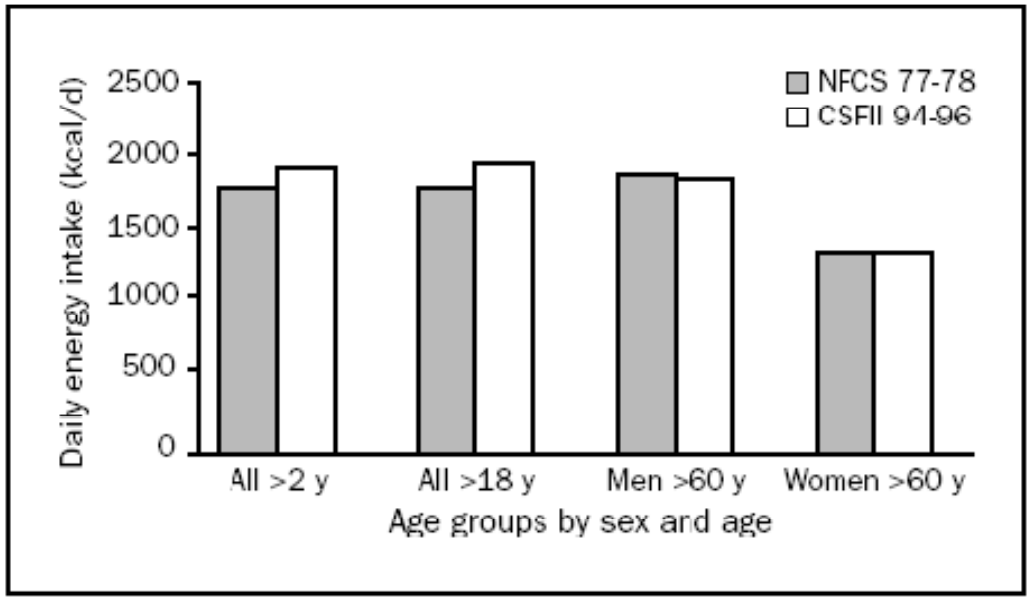


Figure 2. Average daily energy intake in the United States, estimated from the Nationwide Food Consumption Survey (NCFS) in 1977-1978[7] and the Continuing Survey of Food Intakes by Individuals (CFSII) in 1994-1996.[8] Based on data derived from US Department of Agriculture Web site.[6]

La inactividad física aumentó de 46.2% en 2005 a 54.9% en 2009 (p<0.001)

Nivel de actividad física [1]									
	% Total			% Varones			% mujeres		
Total del país	Intenso	Moderado	Bajo	Intenso	Moderado	Bajo	Intenso	Moderado	Bajo
	13,0	32,0	55,0	17,4	31,7	50,9	9,1	32,3	58,6

(1) El nivel de actividad física se constituye a partir de la cantidad de días por semana de actividad física y el tiempo empleado en realizarla

ENFR 2009

FR MORTALIDAD EN EL MUNDO

- HTA : 13%
- Tabaco: 9%
- Diabetes: 6%
- INACTIVIDAD FÍSICA:6% de todas las defunciones

Actividades Sedentarias	kcal	A. Activas	kcal
Uso control remoto	<1	Pararse y cambiar el canal	3
30 min llamadas tel reclinado	4	parado	20
Estacionar lo mas cerca posible	<1	Estacionar, caminar 2 min 5v/sem	8
Contratar personal lavar y planchar	0	Planchar y lavar 30 min c/u	152
Esperar 30 min delivery de pizza	15	Cocinar por 30 min	25
Comprar vegetales congelados	0	Lavar, rebanar y cortar verduras 15 min	10-13
Contratar jardinero	0	Cortar cesped y recoger 30 min c/U	360
Lavadero autos 1/mes	18	Lavar y secar auto manual 1h/mes	300
Dejar salir al perro	2	Sacar al perro a pasear 30 min	135
Manejar 40 min, caminar 5 min (estac)	22	Caminar a la parada colectivo 15 min 2v/d	60
Tomar ascensor 3 pisos	0.3	Caminar	15
Compras on line	30	Caminar 1 hora compras	145-240
Sentado escuchando conferencia 60min	30	Dar una conferencia	70

Evidencia de los Beneficios de AF para la salud

- Prevención Sp y Ob Med Sci Sports Exerc 2007, 39(8): 1423–34: ; Cur Opin Psychiatry 2005, 18: 189–193; Int J Behav Nutr Phys Act 2010, 7: 39
- Prevención DM2 : Am J Epidemiol 1995, 41: 360–8; J Phys Activity Health 2004, 1: 19–28; JAMA 1999, 282: 1433–9; Arch Intern Med 2001, 161: 1542–8; Diabetes Care 2007, 30: 53–8; Diabetes Care 2003, 26: 2918–22; JAMA 2004, 292: 1188–94
- Prevención de enfermedad cardiovascular: Int J ClinPract 2005, 59(8):922–30; ,JAMA 1995, 273: 1093–8; Med Sci Sports Exerc 2007, 39(8): 1423–34; Am J Med 2004, 117: 912–18; N Engl J Med 1986, 314: 605–13
- Prevención enfermedad coronaria: Med Sci Sports Exerc 2007, 39(8): 1423–34; Ann Behav Med 1997, 19(3): 220–9; Int J Behav Nutr Phys Act 2010, 7: 3
- Prevención de cancer: Int J Behav Nutr Phys Act 2010, 7: 39; World Cancer Research Fund / American Institute for Cancer Research, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective (Washington DC: AICR), 2010
- Salud mental: Cur Opin Psychiatry 2005, 18: 189–93; Pub Health Rpts 1985 100(2): 195–201; , Int J Behav Nutr Phys Act 2010, 7: 39

CONCLUSIONES

- Una mejor comprensión de gran parte de los problemas de salud modernos va a ser posible al considerar que la mayor parte de la evolución humana tuvo lugar cuando nuestros ancestros fueron cazadores- recolectores.
  Trevathan WR.
- Estimular la adquisición de hábitos saludables desde el comienzo de la vida es la estrategia más costo-efectiva para la prevención de las enfermedades crónicas no transmisibles

Proteger y promover la salud debe ser un interés prioritario, aún por encima de restablecerla cuando la salud ya está alterada.

Hipócrates

¡¡¡MUCHAS GRACIAS!!!