INFLAMMATORY MECHANISMS IN OBESITY. LINK BETWEEN METABOLIC DISEASES AND OBESITY. POSSIBLE THERAPEUTIC TARGETS.

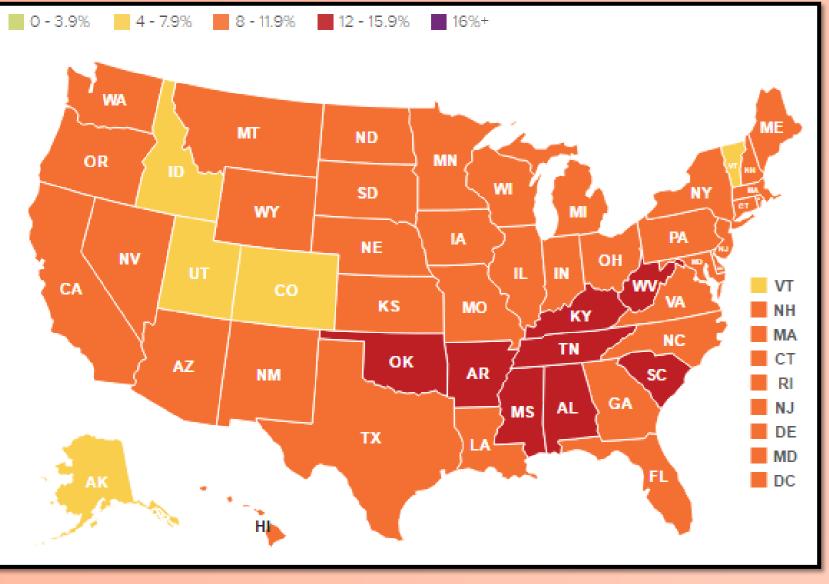
Alejandro Guzmán Pérez – June 2016



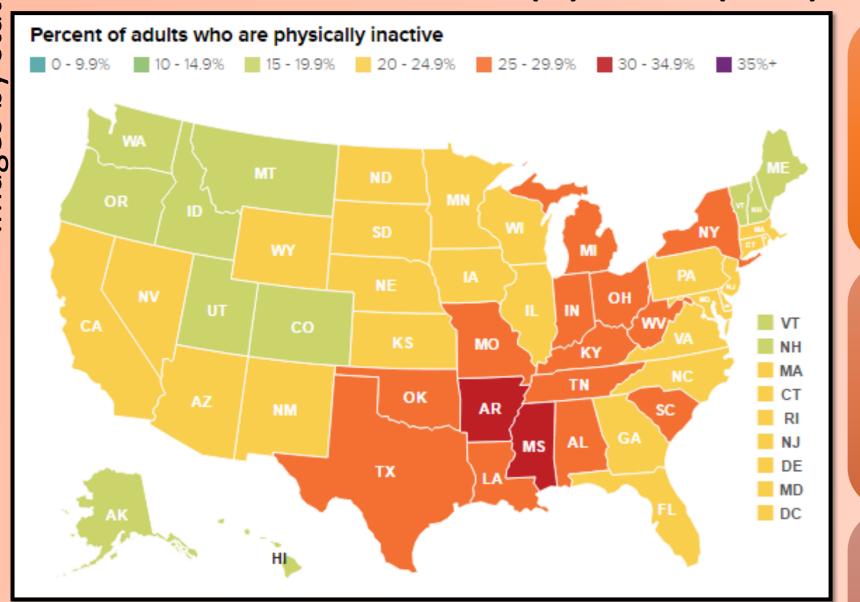
OBESITY AND ITS CONSEQUENCES: WORLDWIDE AND IN THE USA

OBESE ADULTS (%) (IMC > 30) IN USA (2014) ■ 0 - 9.9% ■ 10 - 14.9% ■ 15 - 19.9% ■ 20 - 24.9% ■ 25 - 29.9% ■ 30 - 34.9% ■ 35%+

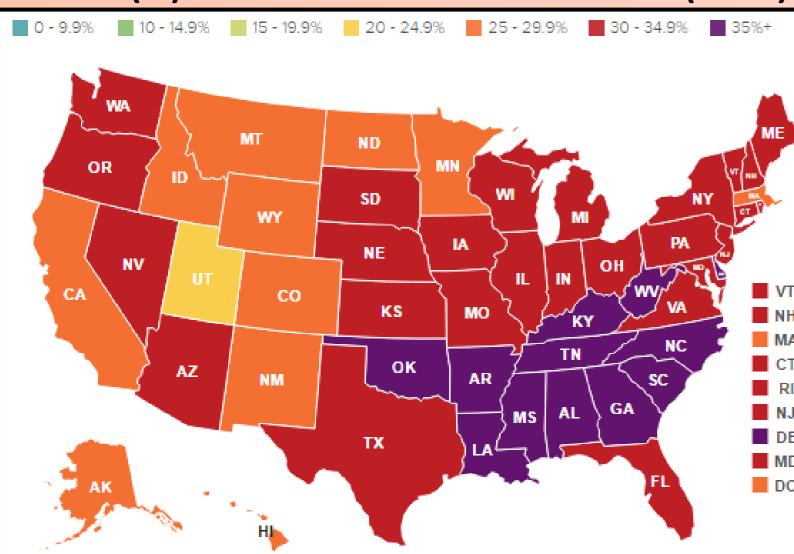
ADULTS (%) WITH DIABETES IN USA (2014)



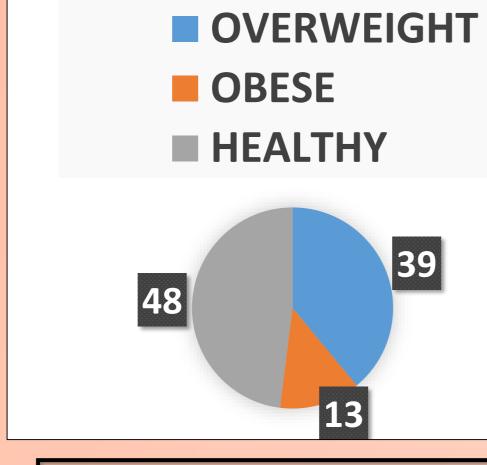
PHYSICALLY INACTIVE ADULTS (%) IN USA (2014)

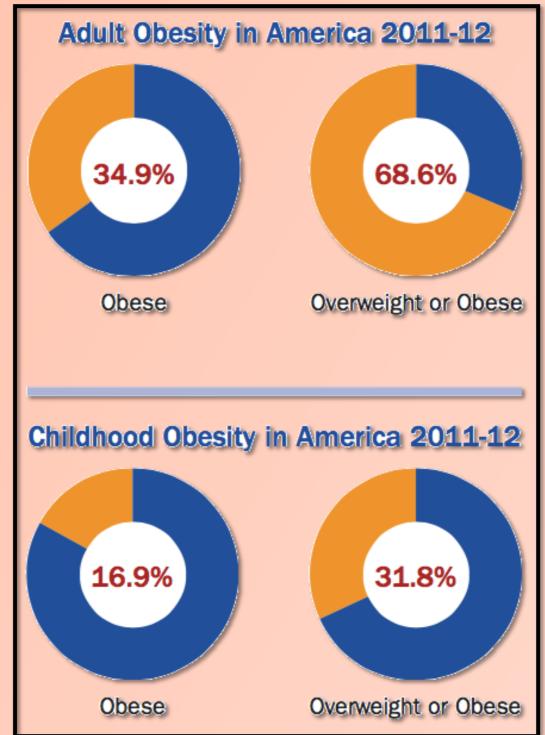


ADULTS (%) WITH HYPERTENSION IN USA (2014)



% OF OVERWEIGHT AND OBESITY WORLDWIDE (2014)





13% of world population is obese. Worldwide obesity has more than doubled since 1980.

39% of adults aged 18 years and over were overweight in 2014, and 13% were obese.

42 million children under the age of 5 were overweight or obese in 2013.

Obesity can lead to several chronic diseases, such as cardiac arrest, hipertensión, diabetes, ostheoarthritis, asma and cancer.

Over a third of americans is obese. Diabetes and hypertension is clearly linked to incidence in obesity.

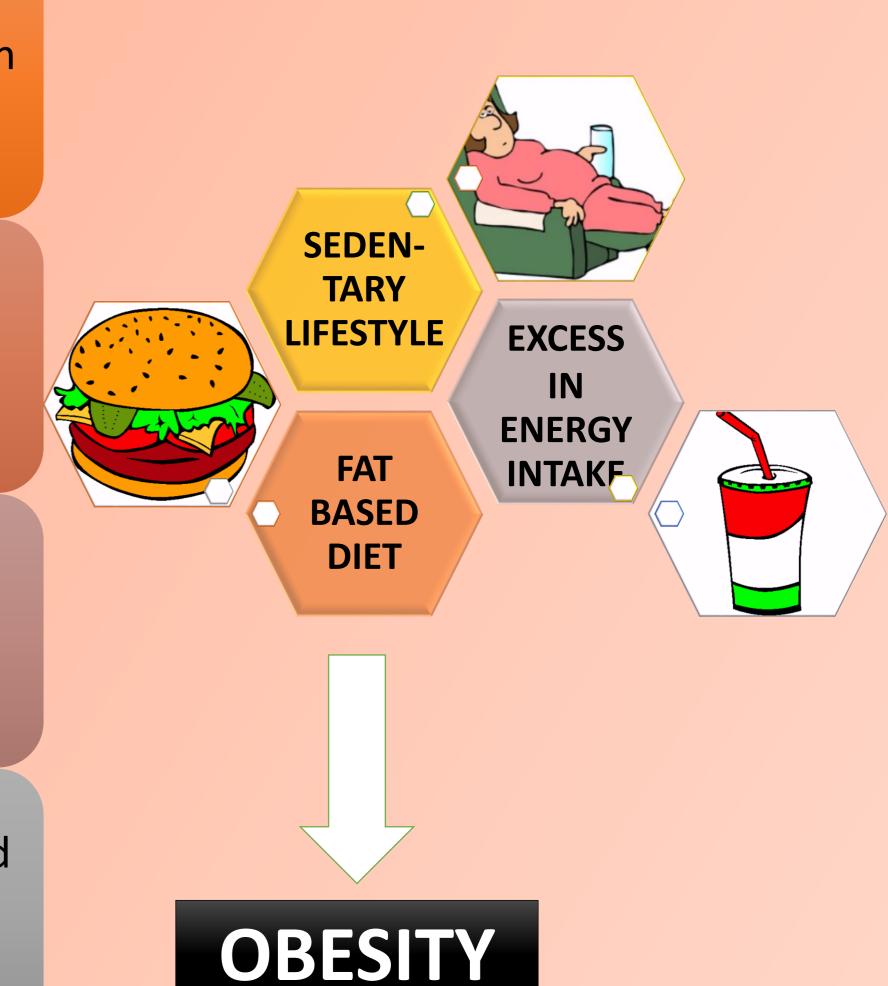
OBESITY AND ITS PRO-INFLAMMATORY EFFECTS

Excessive energy intake, a fat based diet and a sedentary lifestyle are main risk factors for de development of obesity.

Adipose tissue is not merely a fat storing organ: it is a critical component for systemic metabolic and endocrine regulation.

Obesity induces a chronic inflammatory state in metabolic tissues, which has great effect on metabolic tissues.

Inflammation in metabolic tissues causes changes in glucose uptake and insulin sensitivity, promoting the establishment of insulin resistance and diabetes.



Adipose tissue

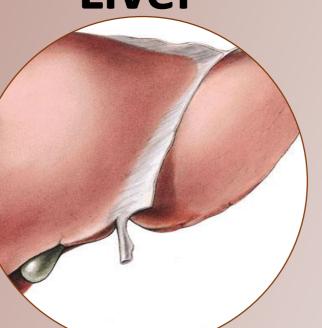


↑ Infiltration of immune cells

↑ Secretion of proinflammatory citokines

↑ M2→M1 inflammatory switch **↓** AMPK ↑ Insulin resistance

Liver



↑ De novo lipogenesis

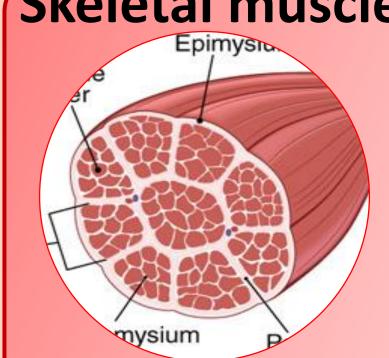
- ↑ Lipid uptake **↑ Glucose output**
- **↓** Lipid oxidation



↓ Insulin secretion **\$\sqrt{\beta}\$ \beta\$-cell function** and mass

↑ Lipidtoxicity **个 Glucotoxicity**

Skeletal muscle



↓ Insulin signaling **↓** Lipid oxidation **↓** Muscle protein

synthesis

↑ Lipid uptake **↑ Lipid Storage**

INFLAMMATION

INSULIN RESISTANCE DIABETES



HOW DOES OBESITY INDUCE INSULIN RESISTANCE?



Excess in plasmatic nutrient concentration (glucose, free fatty acids)

↓ Energy intake regulation by metabolic tissues INSULIN RESISTANCE

个 NLRP3 Inflammasome activity

METABOLIC TISSUES **↓** INSULIN RECEPTOR **SENSITIVITY**

↑ INFLAMMATION IN

↑ Secretion of IL-1beta and promotion of inflammation

CONCLUSIONS

OBESITY IS PREVENTABLE!

IF OBESITY IS PREVENTABLE, DIABETES IS PREVENTABLE.

DIETAND NUTRITION

PHYSICAL ACTIVITY

SPECIFIC ANTI-**INFLAMM ATORY** THERAPY

Prevention of obesity is the key element to the prevention of metabolic disorders.

Antiinflammatory therapy may be helpful in the prevention of metabolic disorders in already obese individuals, as it can impair the development of insulin resistance secondary to inflammation.

Antiinflammatory therapy can not be used as a substitute of obesity prevention.

Prevention of metabolic disorders will therefore be based on a balanced diet, regular physical activity and, in already obese individuals, specific antiinflammatory therapy.