



# Can Adv36 infection lead to overweight and obesity?

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Project title: „Origin and pathogenesis of obesity in relation to non-traditional obesity risk factors“



THE OTHER FLACCO QUARTERBACK |

**SJ**  
MAGAZINE

The Heart of Southern New Jersey

Kids Raised on  
the Registry  
**THE MISTAKES  
OF MEGAN'S  
LAW**

Biking & Hiking  
the Trails of SJ

**Childhood  
OBESITY**  
*Who's to blame?*



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HAS OBAMA SOLD OUT TO THE BANKS?

**Newsweek**

When I  
Grow  
Up, I'm  
Going  
to Weigh  
300 Lbs.  
Help!



MELINDA  
GATE'S BIRTH  
CONTROL  
BOMBHELL  
BILL MAHER  
REMEMBERS  
JOHNNY  
CARSON  
THE RARE  
COURAGE OF  
CHINA'S  
BLIND  
FUGITIVE

Generation  
**Extra  
Large**

Rescuing Our Children from the  
Epidemic of Obesity

Success stories from families fighting the epidemic | How your community can tackle childhood obesity | Surprising — and good — news about junk food and our schools | Plus: A wealth of practical advice from nutrition experts

LISA TARTARELLA, ELAINE WISCHNER, AND CHRIS WOOLSTON



**Newswe**

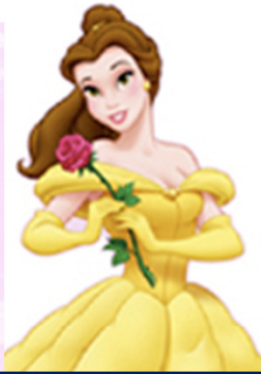
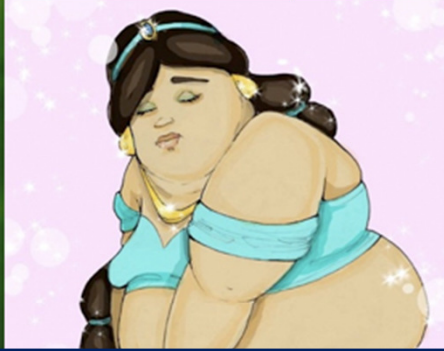
**Fat  
World**

We're Eating  
More Junk  
And Getting  
Less Exercise.

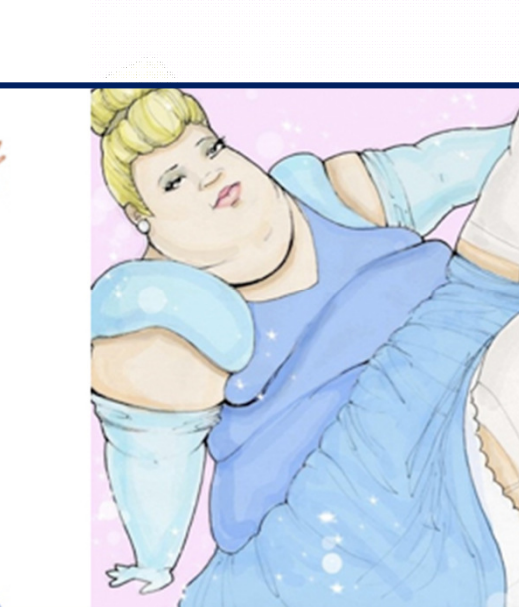
Obesity Is  
The Globe's  
Newest  
Epidemic.

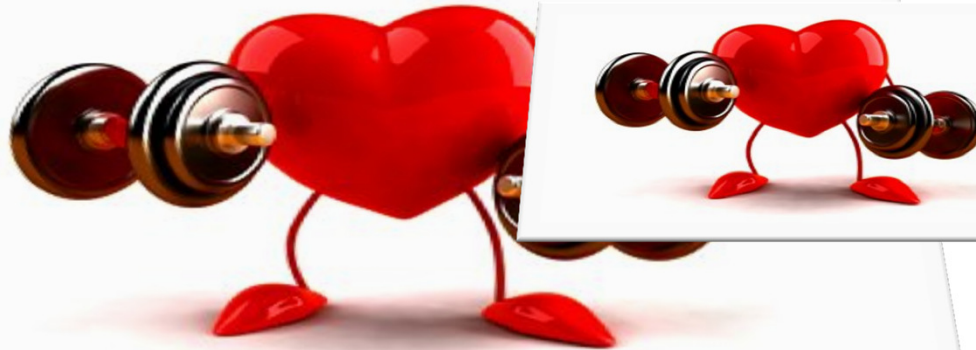






In **2013** the number of overweight children under the age of five, is estimated to be **over 42 million** (31 million of these are living in developing countries)





# Obesity and UA

- !! Associated with a shortened life, because of ↑ risk for cardiovascular disease
- !! 1/3 of obese individuals never develop CV disease; and this group is called the metabolically “healthy” obese
- !! Uric acid levels = marker for metabolically “unhealthy” obesity



# Uric acid and metabolically “unhealthy” obesity

## Our results until now



**We were the first**  
**EAT thickness in children is associated with an unfavorable cardiometabolic risk profile including biochemical signs of NAFLD and hyperuricaemia, but is not a stronger indicator than BMI.**

**In our study UA levels positively correlated with LV diastolic volumes, SV in obese children. It seems that LV volume overload can be influenced by hyperuricemia in presence of obesity.**



Schusterova, I. : Cardiomyopathy associated with obesity: Obesity Cardiomyopathy, In Abdominal Obesity, Risk factors, Weight Reduction and Long- Term Health Effects., *New York : Nova Science Publishers, Inc.*, 2015. ISBN 9781634839501.





**Is Obesity an  
infectious disease?**



# Association of Adenovirus Infection with Human Obesity

Nikhil V. Dhurandhar,\* Pushpa R. Kulkarni,† Sharad M. Ajinkya,‡ Abhaya A. Sherikar,† Richard L. Atkinson\*

JOURNAL OF VIROLOGY, May 1984, p. 301-308  
0022-538X/84/050301-08\$02.00/0

## Specificity of Avian Leukosis Virus-Induced Hyperlipidemia

JEANNE K. CARTER† AND R. E. SMITH‡\*

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Received 11 July 1983/Accepted 7 November 1983

International Journal of Obesity (2005) 29, 281-286  
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www.nature.com/ijo



PAPER

## Human adenovirus-36 is associated with body weight and percentage body fat

R. L. Atkinson<sup>1\*</sup>, N. V. Dhurandhar<sup>2</sup>, P. R. Kulkarni<sup>3</sup>, S. M. Ajinkya<sup>4</sup>, A. A. Sherikar<sup>5</sup>, R. G. Weinsbach<sup>6</sup>, J. M. M. de Groot<sup>6</sup>

Journal of NeuroVirology 8: 1-5, 2002  
© 2002 Taylor & Francis ISSN 1555-0207/02 \$12.00+.00

Mini-Review

## Animal models of postinfectious obesity: Hypothesis and review

MJ Lyons,<sup>1,2</sup> K Nagashima,<sup>3</sup> and R. L. Atkinson<sup>4</sup>

<sup>1</sup>Laboratory of Clinical Microbiology, Life Science, New York University School of Medicine, Saratov, NY

**For over 30 years attention has focused on viral infections (Adenovirus, ...) as a possible etiological factors of obesity**

## Human adenovirus-36 and obesity

R. L. Atkinson

Obetech Obesity Research Center, Richmond, VA, USA

Received 16 December 2011; accepted 21 December 2011

THE EDITOR

THE EDITOR

doi:10.1111/j.2047-6310.2011.00043.x

WORLD OBESITY



# First animal study (Dhurandhar, 2000)

International Journal of Obesity (2000) 24, 989–996  
© 2000 Macmillan Publishers Ltd. All rights reserved 0307-0565/00 \$15.00  
www.nature.com/ijo



## Increased adiposity in animals due to a human virus

NV Dhurandhar<sup>1\*</sup>, BA Israel<sup>2</sup>, JM Kolesar<sup>3</sup>, GF Mayhew<sup>4</sup>, ME Cook<sup>5</sup> and RL Atkinson<sup>6</sup>

<sup>1</sup>Department of Nutrition and Food Science, Wayne State University, Detroit, MI, USA; <sup>2</sup>Department of Pathobiological Sciences, University of Wisconsin, Madison, WI, USA; <sup>3</sup>School of Pharmacy, University of Wisconsin, Madison, WI, USA; <sup>4</sup>Department of Genetics, University of Wisconsin, Madison, WI, USA; <sup>5</sup>Department of Poultry Science, University of Wisconsin, Madison, WI, USA; and <sup>6</sup>Depart

Animals model: **chicken and a mammal**

Results: **Animals inoculated with Adv36 developed a syndrome of increased adipose tissue and paradoxically low levels of serum cholesterol and triglycerides**

# First human study (Atkinson, 2005)

2016  
Cooperation



International Journal of Obesity (2005) 29, 281–286  
© 2005 Nature Publishing Group All rights reserved 0307-0565/05 \$30.00  
www.nature.com/ijo



## PAPER

### Human adenovirus-36 is associated with increased body weight and paradoxical reduction of serum lipids

RL Atkinson<sup>1\*</sup>, NV Dhurandhar<sup>2</sup>, DB Allison<sup>3</sup>, RL Bowen<sup>4</sup>, BA Israel<sup>5</sup>, JB Albu<sup>3</sup> and AS Augustus<sup>6</sup>

**Results: Adv36 is associated with increased body weight and lower serum lipids in humans. Prospective studies are indicated to determine if Adv36 plays a role in the etiology of human obesity**



# Association between obesity and Adv36



**Czech Republic** (*Aldhoon-Hainerova et al, 2014*)

**Korea** (*Na et al, 2010*)

**Mexico** (*Rojas et al, 2013*)

**Turkey** (*Cakmakliogulari et al, 2014*)



**Netherlands and Belgium** (*Goossens et al, 2011*)

**USA** (*Broderick, 2010*)

**Italy** (*Trovato, 2010*)

**Finland** (*Sabin, 2015*)

**South Korea** (*Na, 2012*)

**??? Slovakia**

# Two meta-analyses

## ***Tomohide et al, 2012***

- 10 case-control studies
- Adv36 infection associates with the risk of obesity, but not with abnormal metabolic markers

## ***Shang et al., 2014***

- 11 case-control studies,
- 2508 obese subjects and 3005 controls
- Identified an association between Ad36 infection and a significantly increased risk of obesity development, especially in children





# **Presentation of study results**



# **The aim of this study**

**To assess the relationship between Adv36 seropositivity and the risk of development of obesity and hyperuricemia in children and adolescents**





# Methods

**224** randomly selected students ( $17.72 \pm 1.20$  years of age, 120 female) from **7 high-schools in Kosice** were included in the study.

*Subjects with secondary causes of obesity were excluded and none were taking medications or had a history of cardiovascular disease.*

In 224 healthy students, *anthropometric parameters, fasting plasma glucose and insulin, lipids, uric acid, adipose tissue hormones were measured.* **Adv36 antibody** was detected by ELISA test.

# Healthy high-school students in Eastern Slovakia- Our results



**Prevalence of  
overweight and obesity**

**23.66%**

## Biochemical characteristics of overweight/obese and lean control study groups

Antropometric and biochemical parameters	Normal weight Mean $\pm$ SD N=171	Obese and overweight Mean $\pm$ SD N=53	p- value
<b>Age (years)</b>	<b>17.74 <math>\pm</math> 1.16</b>	<b>17.67 <math>\pm</math> 1.34</b>	<b>0.73</b>
<b>Body weight (kg)</b>	<b>61.84 <math>\pm</math> 9.59</b>	<b>85.16 <math>\pm</math> 16.33</b>	<b>&lt;0.0001</b>
<b>Body height (cm)</b>	<b>172.64 <math>\pm</math> 9.99</b>	<b>173.55 <math>\pm</math> 10.33</b>	<b>0.56</b>
<b>WHR</b>	<b>0.79 <math>\pm</math> 0.06</b>	<b>0.89 <math>\pm</math> 0.07</b>	<b>&lt;0.0001</b>
<b>Body fat mass (kg)</b>	<b>11.09 <math>\pm</math> 4.45</b>	<b>24.70 <math>\pm</math> 10.89</b>	<b>&lt;0.0001</b>
<b>Body muscle mass (kg)</b>	<b>26.98 <math>\pm</math> 6.41</b>	<b>33.69 <math>\pm</math> 7.35</b>	<b>&lt;0.01</b>
<b>Body fat percentile (%)</b>	<b>19.00 <math>\pm</math> 7.51</b>	<b>29.00 <math>\pm</math> 10.59</b>	<b>&lt;0.01</b>
<b>Visceral fat mass (cm<sup>2</sup>)</b>	<b>62.83 <math>\pm</math> 60.65</b>	<b>167.36 <math>\pm</math> 144.67</b>	<b>&lt;0.0001</b>
<b>Basal metabolic rate (kcal)</b>	<b>1420.82 <math>\pm</math> 231.26</b>	<b>1659.92 <math>\pm</math> 262.11</b>	<b>&lt;0.01</b>

WHR: Waist to Hip Ratio



## Anthropometric characteristics of overweight/obese and lean control study groups

Antropometric and biochemical parameters	Normal weight Mean $\pm$ SD N=171	Obese and overweight Mean $\pm$ SD N=53	p- value
<b>Glucose (mmol L<sup>-1</sup>)</b>	<b>4.47 <math>\pm</math> 0.57</b>	<b>4.75 <math>\pm</math> 0.74</b>	<b>&lt;0.05</b>
<b>Uric acid (umol L<sup>-1</sup>)</b>	<b>292.23 <math>\pm</math> 59.86</b>	<b>341.62 <math>\pm</math> 70.72</b>	<b>&lt;0.0001</b>
<b>AST (ukat L<sup>-1</sup>)</b>	<b>0.41 <math>\pm</math> 0.27</b>	<b>0.43 <math>\pm</math> 0.18</b>	<b>0.74*</b>
<b>ALT (ukat L<sup>-1</sup>)</b>	<b>0.35 <math>\pm</math> 0.21</b>	<b>0.43 <math>\pm</math> 0.26</b>	<b>&lt;0.01</b>
<b>Total cholesterol (mmol L<sup>-1</sup>)</b>	<b>4.11 <math>\pm</math> 0.68</b>	<b>4.14 <math>\pm</math> 0.70</b>	<b>0.82</b>
<b>TAG (mmol L<sup>-1</sup>)</b>	<b>0.88 <math>\pm</math> 0.46</b>	<b>1.07 <math>\pm</math> 0.67</b>	<b>&lt;0.01</b>
<b>HDL cholesterol (mmol L<sup>-1</sup>)</b>	<b>1.56 <math>\pm</math> 0.31</b>	<b>1.33 <math>\pm</math> 0.27</b>	<b>&lt;0.0001</b>
<b>LDL cholesterol (mmol L<sup>-1</sup>)</b>	<b>2.35 <math>\pm</math> 0.50</b>	<b>2.49 <math>\pm</math> 0.58</b>	<b>0.08</b>
<b>hsCRP (mg L<sup>-1</sup>)</b>	<b>0.79 <math>\pm</math> 0.80</b>	<b>1.63 <math>\pm</math> 1.59</b>	<b>&lt;0.0001</b>
<b>Inzulin (uIU/ml)</b>	<b>10.44 <math>\pm</math> 10.01</b>	<b>16.39 <math>\pm</math> 16.83</b>	<b>&lt;0.001</b>
<b>Adiponectin (ng/ml)</b>	<b>9.49 <math>\pm</math> 5.05</b>	<b>6.91 <math>\pm</math> 3.11</b>	<b>&lt;0.001</b>
<b>Rezistin (ng/ml)</b>	<b>7.74 <math>\pm</math> 3.92</b>	<b>8.27 <math>\pm</math> 3.80</b>	<b>0.29*</b>
<b>Leptin (ng/ml)</b>	<b>5.80 <math>\pm</math> 6.20</b>	<b>15.94 <math>\pm</math> 16.66</b>	<b>&lt;0.0001</b>
<b>Ghrelin (pg/ml)</b>	<b>910.38 <math>\pm</math> 267.48</b>	<b>861.22 <math>\pm</math> 310.72</b>	<b>&lt;0.05</b>
<b>HOMA-index</b>	<b>2.13 <math>\pm</math> 2.35</b>	<b>3.77 <math>\pm</math> 4.79</b>	<b>&lt;0.001</b>

HOMA index: homeostasis model assessment of insulin resistance, AST: aspartate aminotransferase, ALT: alanine aminotransferase, TAG: triacylglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein, hsCRP: high-sensitivity C-reactive protein

## Anthropometric characteristics of Adv36 negative/ Adv36 positive study groups

Anthropometric parameters	Adv36 negative Mean $\pm$ SD N= 164	Adv36 positive Mean $\pm$ SD N= 60	p-value
Age (years)	17.62 $\pm$ 1.27	18.010 $\pm$ 0.94	0.06
Body weight (kg)	66.88 $\pm$ 16.21	68.67 $\pm$ 12.01	0.12
Body height (cm)	171.95 $\pm$ 10.16	175.33 $\pm$ 9.32	<0.05
BMI	22.47 $\pm$ 4.39	22.23 $\pm$ 3.12	0.87
BMI percentil	53.55 $\pm$ 32.48	51.91 $\pm$ 29.92	0.73
WHR	0.82 $\pm$ 0.08	0.80 $\pm$ 0.08	0.24
Body fat mass (kg)	15.66 $\pm$ 10.45	15.09 $\pm$ 6.24	0.87
Body musle mass (kg)	28.24 $\pm$ 6.92	32.23 $\pm$ 8.33	0.13
Body fat percentile (%)	22.58 $\pm$ 10.08	21.16 $\pm$ 8.91	0.68

BMI: Body Mass Index, WHR: Waist to Hip Ratio

## Biochemical characteristics of Adv36 negative/ Adv36 positive study groups

Biochemical parameters	Ad36 negative Mean $\pm$ SD N= 164	Ad36 positive Mean $\pm$ SD N= 60	p-value
Glucose (mmol L <sup>-1</sup> )	4.55 $\pm$ 0.63	4.48 $\pm$ 0.60	0.48
Uric acid (umol L <sup>-1</sup> )		???	
AST (ukat L <sup>-1</sup> )	0.42 $\pm$ 0.28	0,39 $\pm$ 0.12	0.94
ALT (ukat L <sup>-1</sup> )	0.37 $\pm$ 0.25	0.35 $\pm$ 0.13	0.55
Total cholesterol (mmol L <sup>-1</sup> )	4.15 $\pm$ 0.66	4.03 $\pm$ 0.74	0.23
TAG (mmol L <sup>-1</sup> )	0.95 $\pm$ 0.54	0.85 $\pm$ 0.45	0.19
HDL cholesterol (mmol L <sup>-1</sup> )	1.50 $\pm$ 0.32	1.51 $\pm$ 0.28	0.95
LDL cholesterol (mmol L <sup>-1</sup> )	2.39 $\pm$ 0.51	2.36 $\pm$ 0.55	0.72
hsCRP (mg L <sup>-1</sup> )	1.074 $\pm$ 1.20	0.78 $\pm$ 0.74	0.23
Inzulin (uIU/ml)	12.61 $\pm$ 13.32	9.86 $\pm$ 8.34	0.16
HOMA-index	2.69 $\pm$ 3.45	2.08 $\pm$ 2.27	0.22

HOMA index: homeostasis model assessment of insulin resistance, AST: aspartate aminotransferase, ALT: alanine aminotransferase, TAG: triacylglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein, hsCRP: high-sensitivity C-reactive protein



# Adv36 infection and UA

**First study focusing on the assessment of the relation of Adv36 infection and hyperuricemia**

Multiple regression analyses dependent variable: UA				
N=224	beta	B	t (221)	p-value
		154.12	6.81	<0.0001
BMI	0.39	6.42	6.52	<0.0001
Ad36	0.14	21.89	2.41	<0.05

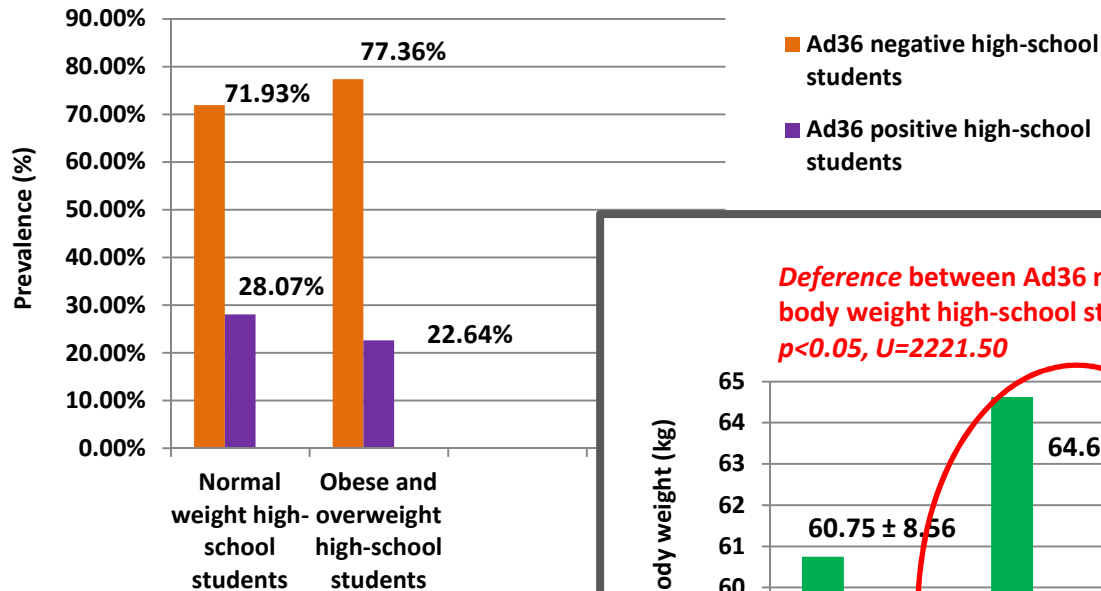
**UA=6,42\*BMI + 21,9\*Adenovirus + 154,12**

Biochemical parameters	Ad36 negative Mean ± SD N= 164	Ad36 positive Mean ± SD N= 60	p-value
<b>Uric acid (UA) (umol L<sup>-1</sup>)</b>	<b>298.45 ± 63.05</b>	<b>318.79 ± 71.51</b>	<b>&lt;0.05</b>

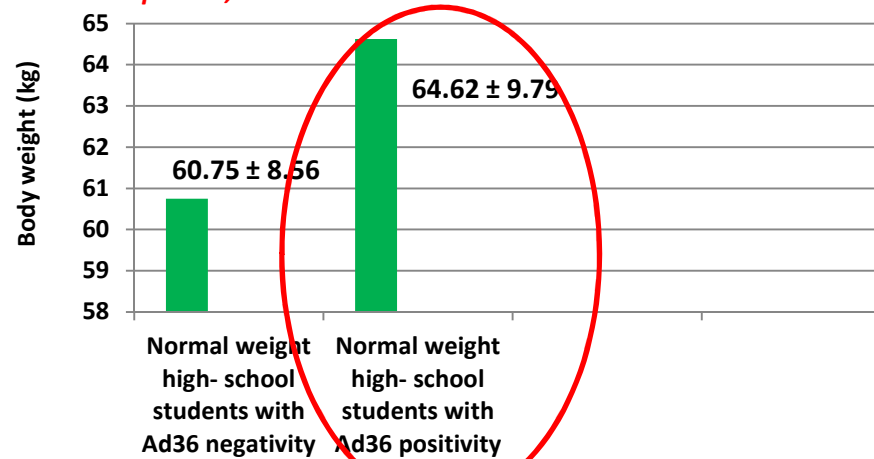
**We confirmed the association between the elevated UA levels and Adv36 seropositivity in adolescents**

# Influence of Adv36 on body weight

Differences between normal and obese and overweight high-school students in prevalence of Adv36 positivity (chi-kv: 0.60, p=0.43)



Deference between Adv36 negative and Adv36 positive normal body weight high-school students in body weight p<0.05, U=2221.50

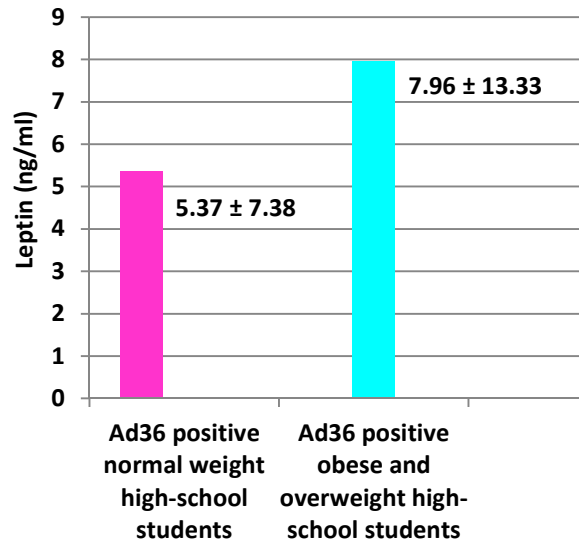


**Adv36 seropositivity was associated with higher body weight in normal weight students**

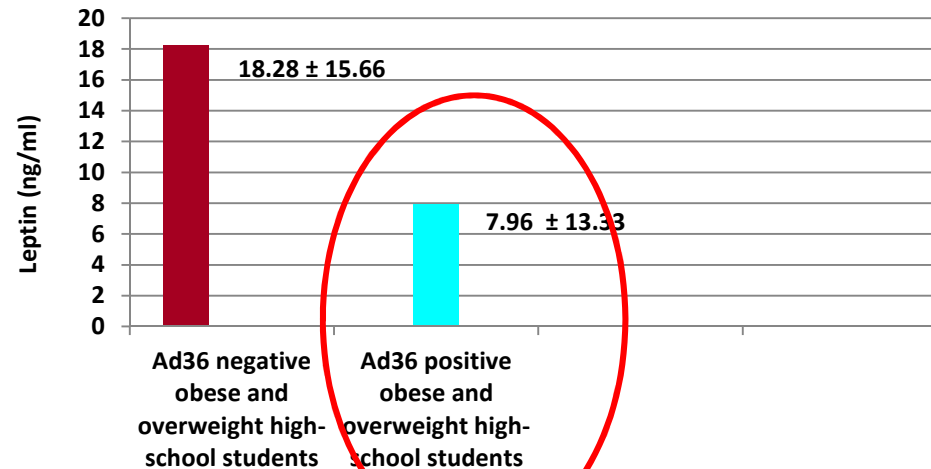
# Influence of Adv36 on serum leptin level

**It seems that Adv36 infection is associated with leptin secretion independently of the presence of obesity in adolescents**

Differences between Adv36 positive normal weight and obese and overweight high-school students in serum leptin levels ( $p=0.27$ ,  $U=229.00$ )



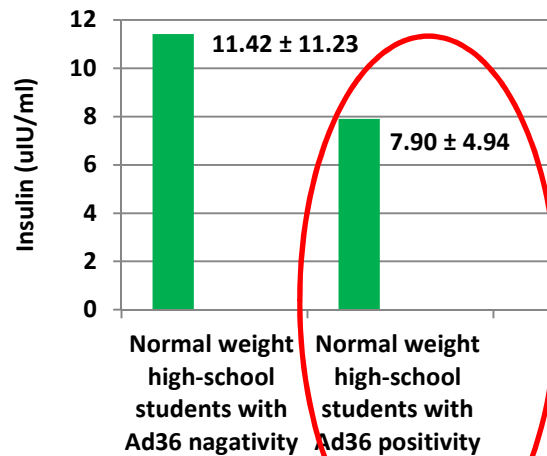
Differences between Adv36 negative and Adv36 positive obese and overweight high-school students in serum leptin levels ( $p<0.01$ ,  $U=122.50$ )



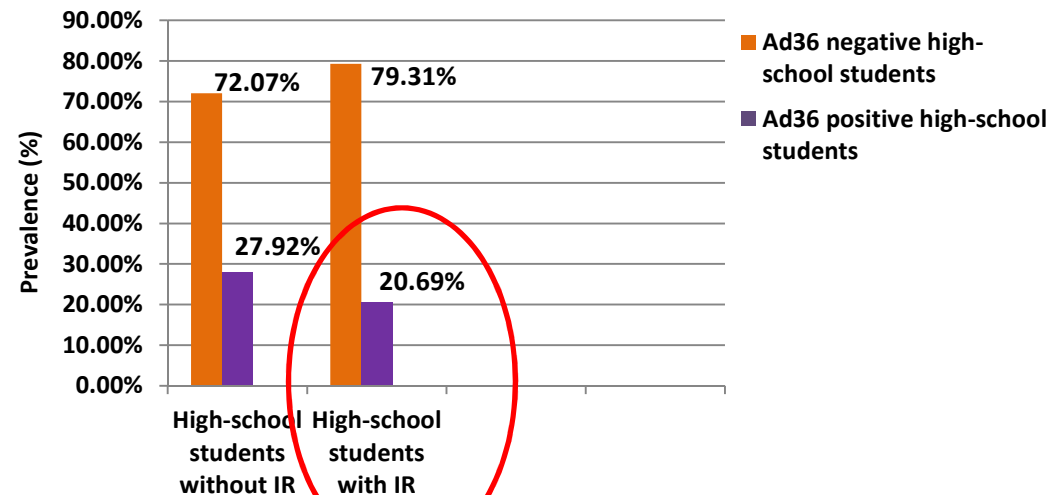


# Prevalence of Adv36 infection in study groups

*Deference between Ad36 negative and Ad36 positive normal weight high-school students in serum Insulin levels*  
 $p < 0.07$ ,  $U = 2051.00$



*Differences between high-school students with and without IR in prevalence of Adv36 positivity (chí-kv: 0.66,  $p = 0.41$ )*



**Adv36 adipogenic adenovirus effect on body composition is not operating through an insulin-resistance-related mechanism**



# CONCLUSION

**Our study suggest possible direct influence of Adv36 infection on development or progression of unhealthy obesity and CV risk**

**The study demonstrates a relationship between Adv36 infection and the risk of development of obesity in normal weight children and adolescents**

**We did not find higher prevalence of Adv36 seropositivity in obese adolescents**



**Virulence factors of adenovirus could be changed during the time ??? ...**

**Other bacterias / viruses??? ...**

**Further studies are required to elucidate this biological mechanism of such complex relationship**

*The End*



*Ending Childhood Obesity*