

XVII Giornate Pediatriche Salernitane



OBESITÀ ED ASMA

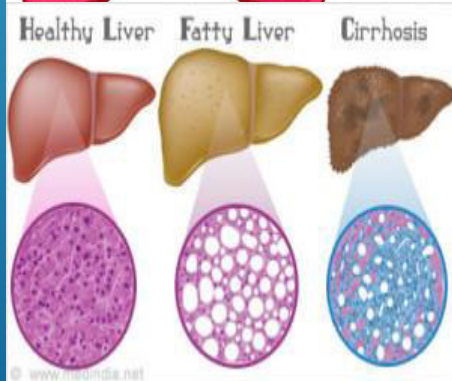
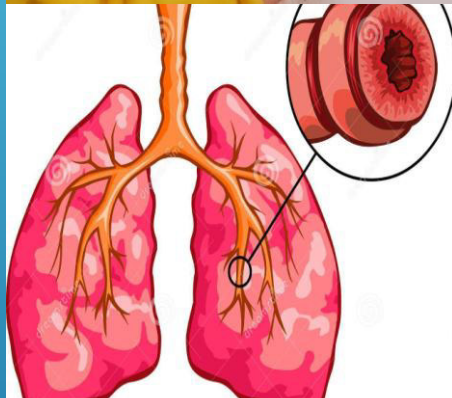
Pietro VAJRO

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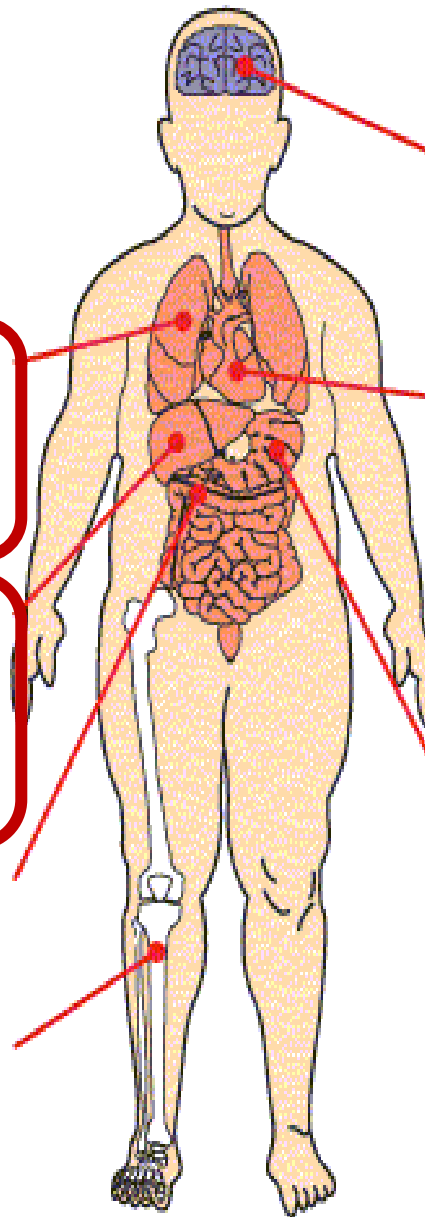
Psychosocial
 Eating disorders
 Poor self-esteem
 Body image disorder
 Social isolation and stigmatisation
 Depression

Pulmonary
 Exercise intolerance
 Obstructive sleep apnoea
 Asthma

Gastrointestinal
 Gallstones
 Gastro-oesophageal reflux
Non-alcoholic fatty liver disorder

Renal
 Glomerulosclerosis

Musculoskeletal
 Ankle sprains
 Flat feet
 Tibia vara
 Slipped capital femoral epiphysis
 Forearm fracture



Neurological
 Pseudotumour cerebri
 (idiopathic intracranial hypertension)

Cardiovascular
 Hypertension
 Dyslipidaemia
 Coagulopathy
 Chronic inflammation
 Endothelial dysfunction

Endocrine
 Insulin resistance
 Impaired fasting glucose
 or glucose intolerance
 Type 2 diabetes
 Precocious puberty
 Menstrual irregularities
 Polycystic ovary
 syndrome (females)

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syndrome (females)

Normal
breathing

Snoring - Partial
obstruction
of the airway

OSA - Complete
obstruction
of the airway

Tongue

Soft palate
Uvula



Healthy Liver

Fatty Liver

Cirrhosis



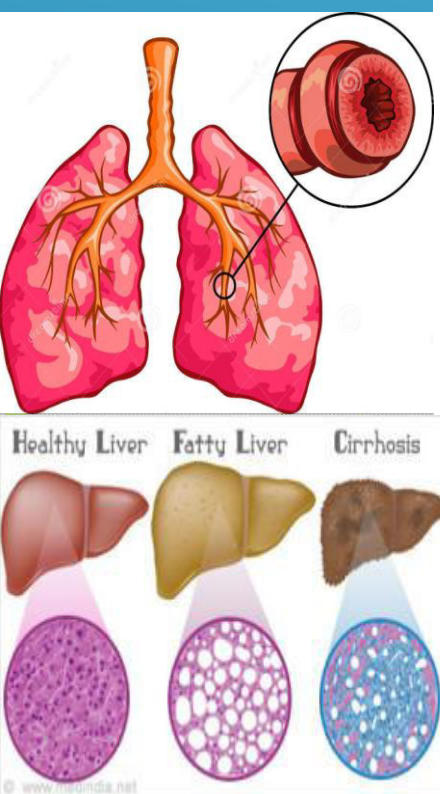
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H Gordon, P Patel, J Hull, K Nimako and A Menzies-Gow

Gut 2013 62: A89-A90

doi: 10.1136/gutjnl-2013-304907.197

Updated information and services can be found at:

http://gut.bmj.com/content/62/Suppl_1/A89.3

Severe asthma may entail frequent corticosteroid use and a sedentary lifestyle; both predispose to risk factors implicated in NAFLD. As such we hypothesised a link between asthma and NAFLD, and a possible under detection of NAFLD amongst patients with severe asthma.

Methods We audited the investigation and management of NAFLD amongst patients under the care of the Difficult Asthma Team at the Royal Brompton Hospital. We conducted a retrospective study of patients who were entered into the National Asthma Database following investigations under the Difficult Asthma Protocol (DAP) between 2007 and 2011. The following were included: Age at diagnosis, liver function (at initial assessment and most recent), liver imaging, glucose and lipids at initial investigation, and medication history.

Results 209 subjects were included in the audit, all of whom entered into the National Asthma Database between 2007 and 2011. Mean age was 45 at presentation to RBH.

Abnormal Liver Function 20% (n = 41) patients had abnormal liver function tests either at first presentation to RBH or on their most recent blood tests. Only 14 (34%) were further investigated with liver imaging. Of those with deranged liver function who were imaged, 79% (n = 11) had radiological evidence of NAFLD.

Management of patients with confirmed NAFLD Of the patients with confirmed NAFLD only 27% (n = 3) had their fasting lipids and glucose measured. 18% (n = 2) were prescribed a statin and a similar number were prescribed metformin.

Asthma medications of patients subsequently diagnosed with NAFLD 81% of patients were prescribed aminophylline. 54% were prescribed montelukast and 81% patients were prescribed oral corticosteroids. 36% of patients were treated with omalizumab (anti IgE).

Conclusion Amongst our cohort of **severe asthmatics** substantial proportion have deranged liver function. Of those with abnormal LFT who underwent imaging, a high proportion (79%) had radiological evidence of NAFLD. However 66% of patients with deranged LFT did not proceed to liver imaging. This suggests that NAFLD is currently under diagnosed and managed in this patient population

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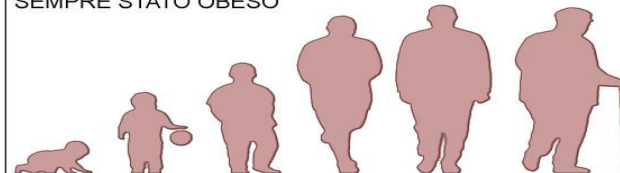
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Endothelial dysfunction

Endocrine

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Impaired fasting glucose
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syndrome (females)

SEMPRE STATO OBESO



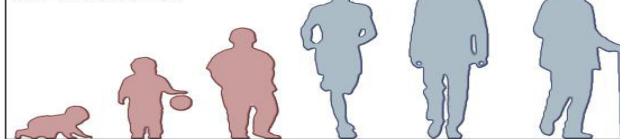
RISCHIO AUMENTATO
DI SVILUPPARE MALATTIE
LEGATE ALL'OBESITÀ

SEMPRE STATO NORMOPESO



RISCHIO NORMALE
DI SVILUPPARE MALATTIE
LEGATE ALL'OBESITÀ

DA OBESO, A NORMOPESO
IN ETÀ ADULTA



Clinical presentation of obese asthma:

→ distinct from other asthma
phenotypes

→ tends to be more severe,

→ not typically associated
with allergy,

→ < responsive to std
therapy, including steroids

OBESITY AND THE RESPIRATORY SYSTEM DISEASES

Affects the respiratory system health adversely in more ways than one.

- **Exertional dyspnea** – This is basically severe breathlessness caused due to minor exertions. This is a common feature among obese individuals.
- **Obstructive sleep apnea syndrome (OSAS)** ← to closing or narrowing of the airways during sleep leading to snoring, repeated waking and lack of adequate and restful sleep → S Pickwick ...
- **Chronic obstructive pulmonary disease (COPD)**
- **Obesity hypoventilation syndrome** ← Obese individuals = low lung reserve & difficulty in providing enough O₂ for their body → hypoxia.
- **Pulmonary embolism** = a life threatening medical emergency → failure and death.

ASTHMA – Obese are more at risk of **asthma exacerbations**.

Studies show that:

- prevalence of asthma is higher by
 - 38% in overweight patients
 - 92% in obese patients.
- Obese patients with asthma
 - get more acute attacks,
 - need more asthma medication,
 - need more frequent visits to ED
 - have more hospital admissions than non obese patients with asthma.



Associazione ancora molto dibattuta **obesità e asma:**

- **prevalenza di entrambe è aumentata** in adulti e bambini
- studi indicano associazione tra **BMI e sintomi di asma/wheezing.**

QUESITO 1 → i bambini **obesi** sono più **predisposti**

- ad avere l'**asma** ?
- o più semplicemente ad avere una **Mal. Respiratoria** con
 - > **sensibilità vie aeree** periferiche (perchè di < calibro)?
 - sintomi simili a quelli dell'asma (respiro sibilante, tosse, dispnea, senso di costrizione toracica) scatenati da altri fattori (es.: RGE), **reversibile con perdita peso?**

QUESITO 2

- è l'**asma che predispone all'obesità** riducendo capacità di svolgere attività fisica ?

IPOTESI : maggior frequenza di sintomi asmatici nel bambino obeso spiegata anche da fattori correlati allo stile di vita ?

- **ridotta attività fisica**: l'esercizio aerobico attenua l'entità della flogosi bronchiale nell'animale da esperimento sensibilizzato all'ovoalbumina ed esposto ad aerosol con questa sostanza; inoltre, diminuisce il livello di IgE specifiche e riduce la traslocazione nucleare di NFkb,
- **dieta scorretta, carente in acidi grassi buoni come gli omega3** (olio di pesce → riduce la comparsa di segni respiratori nei bambini asmatici).



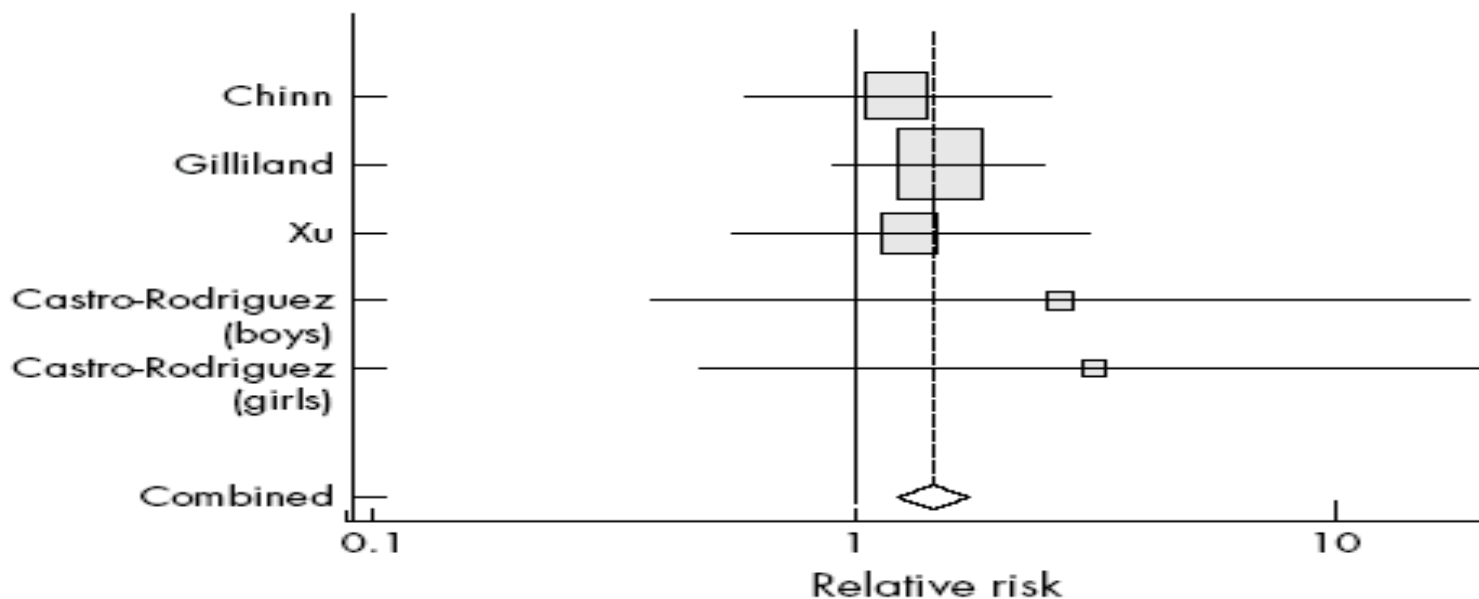
Una recente meta-analisi (*Arch Dis Child*;Apr) ha fornito una stima del **rischio di sviluppare asma nei bambini in sovrappeso ($\text{BMI} \geq 85^{\circ}$) e nei bambini con elevato peso alla nascita ($\geq 3,8$ kg oppure Ponderal Index $\geq 2,5$ g/cm³ o ≥ 27 kg/m²);**

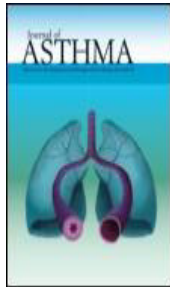
il lavoro, che ha combinato i risultati di 12 studi

- 9 riguardanti l'effetto peso elevato nascita \rightarrow sviluppo asma

- 4 la correlazione sovrappeso in età scolare \rightarrow outcome asma,

\rightarrow ha concluso che **l'eccesso ponderale nei bambini in età scolare aumenta il rischio di sviluppare asma di circa il 50% ($\text{RR}=1,5$)**



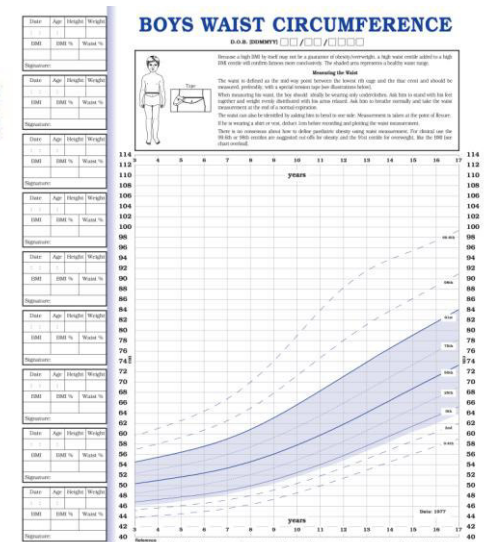
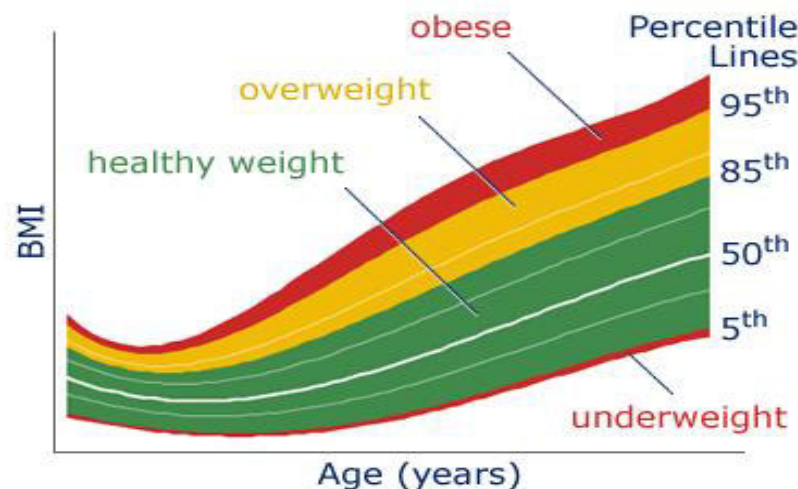


Obesity

Associations between central obesity and asthma in children and adolescents: a case-control study

Constantina Papoutsakis PhD, RD^{ab*}, Maria Chondronikola

Conclusions: Presence of **central obesity** and high-body weight (at least overweight) as assessed by waist circumference, waist-to-height ratio, and BMI are associated with asthma diagnosis.

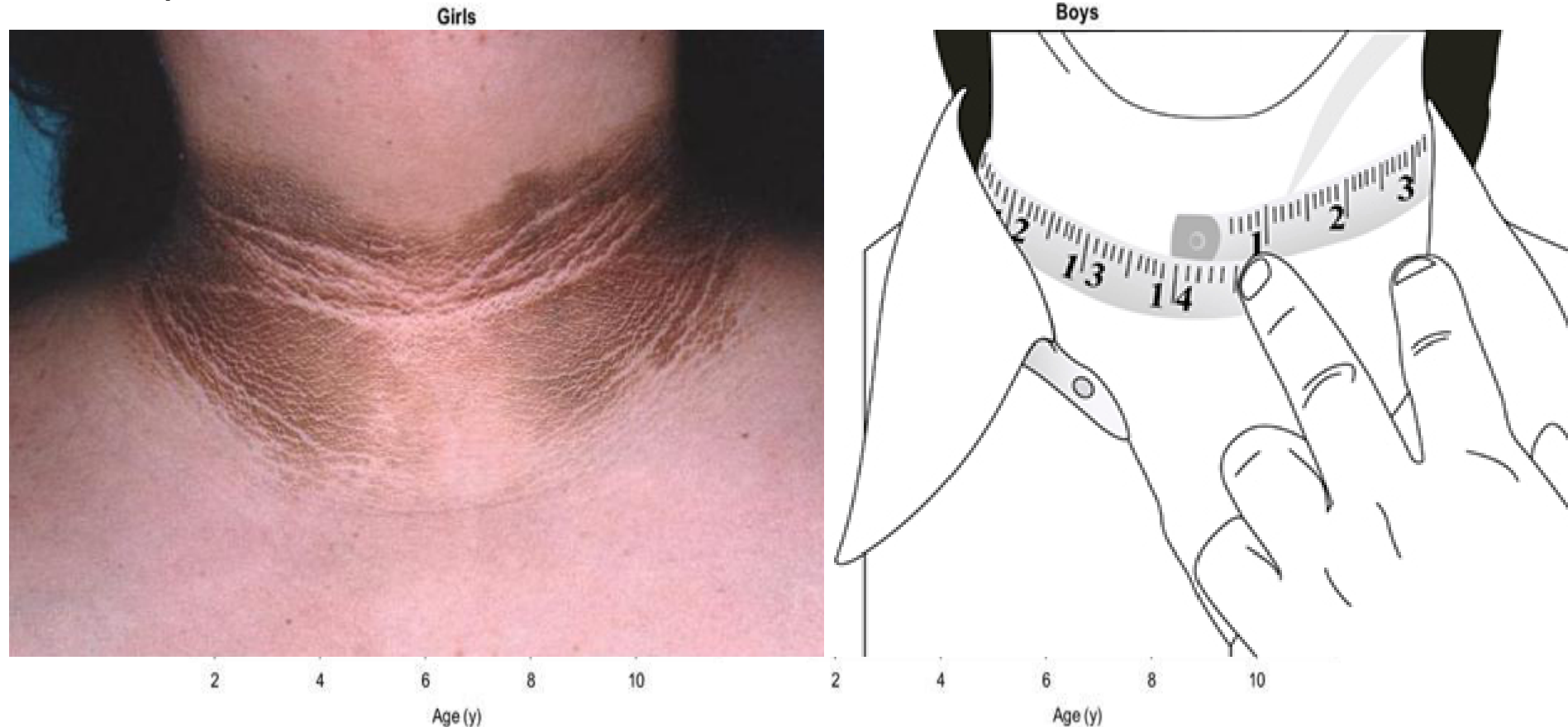


FROM:
Percentile reference values for anthropometric body composition indices in European children from the IDEFICS study

P Nagy, et al

Figure 6.

Percentile curves of neck circumference in normal-weight European girls and boys.



Ann Allergy Asthma Immunol 2016 Jun;116(6):514-7

Association of wider neck circumference (NC) and asthma in obese children.

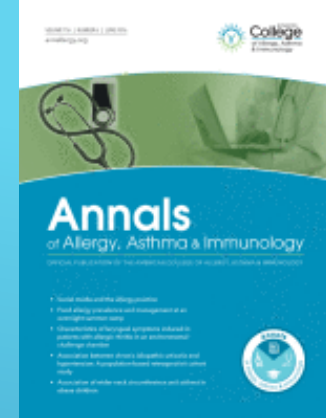
Akin O, Sari E, Arslan M, Yeşilkaya E

METHODS:

- School age children with **asthma**
- **Controls** with allergic symptoms, such as rhinitis, urticaria and atopic dermatitis.

RESULTS:

- A total of 196 children (92 male [46.9%])
- Asthma was present in 102 patients (52.1%).
 - Ninety-one of the pts (46.4%) were OW, and 45 pts (22.9%) were OB
 - NC of children with asthma was significantly > than that of ctrls.
 - the prevalence of children with a NC > the 90th percentile (grade 6) was more frequent when compared with ctrls.
 - The median NC of OB-OW with asthma was significantly higher compared with OB-OW controls without asthma.
 - multivariable logistic regression → presence of a NC in the greater than 90th percentile was associated with asthma in OB-OW children.
 - NC, is associated with asthma in OB children.



Pediatr Allergy Immunol. 2015 Aug;26(5):456-60.

WIDER NECK CIRCUMFERENCE (NC) IS RELATED TO SEVERE ASTHMA IN CHILDREN.

Hacihamdioglu B, Arslan M, Yeşilkaya E, Gok F, Yavuz ST.

METHODS:

Children with asthma . Asthma severity was graded according to GINA

Group1 (mild asthma) = children with asthma controlled with Step 1- 2

Group 2 (moderate-to- severe asthma) = children needing Step 3, 4, 5

Anthropometric measures.

RESULTS:

127 children [8.3 yrs (6.4-11.3)] → Atopy was present in 77 (60.6%) pts

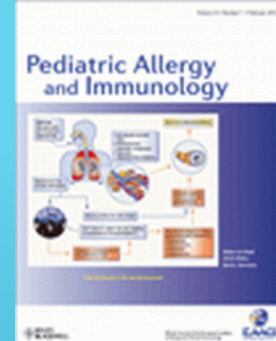
91 pts (71.6) were in the mild asthma group.

NC of children with severe asthma was significantly > children with mild asthma (29.0 cm (27.0-32.0) vs. 28.0 (26.0-30.0), $p = 0.019$).

The prevalence of children with NC > 90th %ile more frequent in children with severe asthma (15 [41.7%] vs. 21 [23.1%]).

Presence of NC > 90th %ile → associated with severe asthma (OR 2.52 [1.05-6.01]; $p = 0.038$).

CONCLUSIONS: NC associated with asthma severity in children.



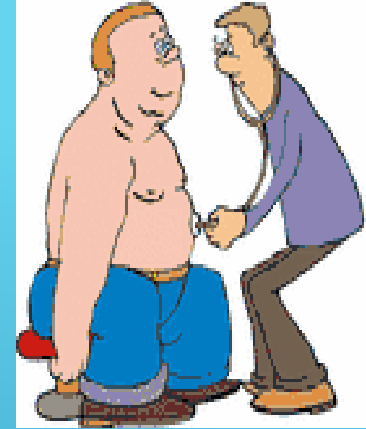
ASTHMA AND OBESITY

OBESITY IS AN INDEPENDENT RISK FACTOR FOR ASTHMA.

OBESITY MAY INFLUENCE ON AIRWAY HYPER-RESPONSIVENESS AND IS CAPABLE OF REDUCING

- pulmonary compliance
- lung volumes
- the diameter of peripheral respiratory airways

INCREASED ADIPOSE TISSUE



→ SYSTEMIC INFLAMMATORY STATE

→ RISE OF SERUM CONCENTRATIONS OF

- **proinflammatory adipokines** (leptin, resistin)
- **antiinflammatory adipokines** (adiponectin)

→ may be causally associated with asthma, however human studies are inconclusive.

→ INCREASED ASTHMA SEVERITY AND RELATIVE CORTICOSTEROID RESISTANCE.

→ Some studies suggest **improvements in the disease with weight loss** in obese asthma patients.

Recently published data suggest that **obese asthma patients may represent a **distinct phenotype of asthma.****

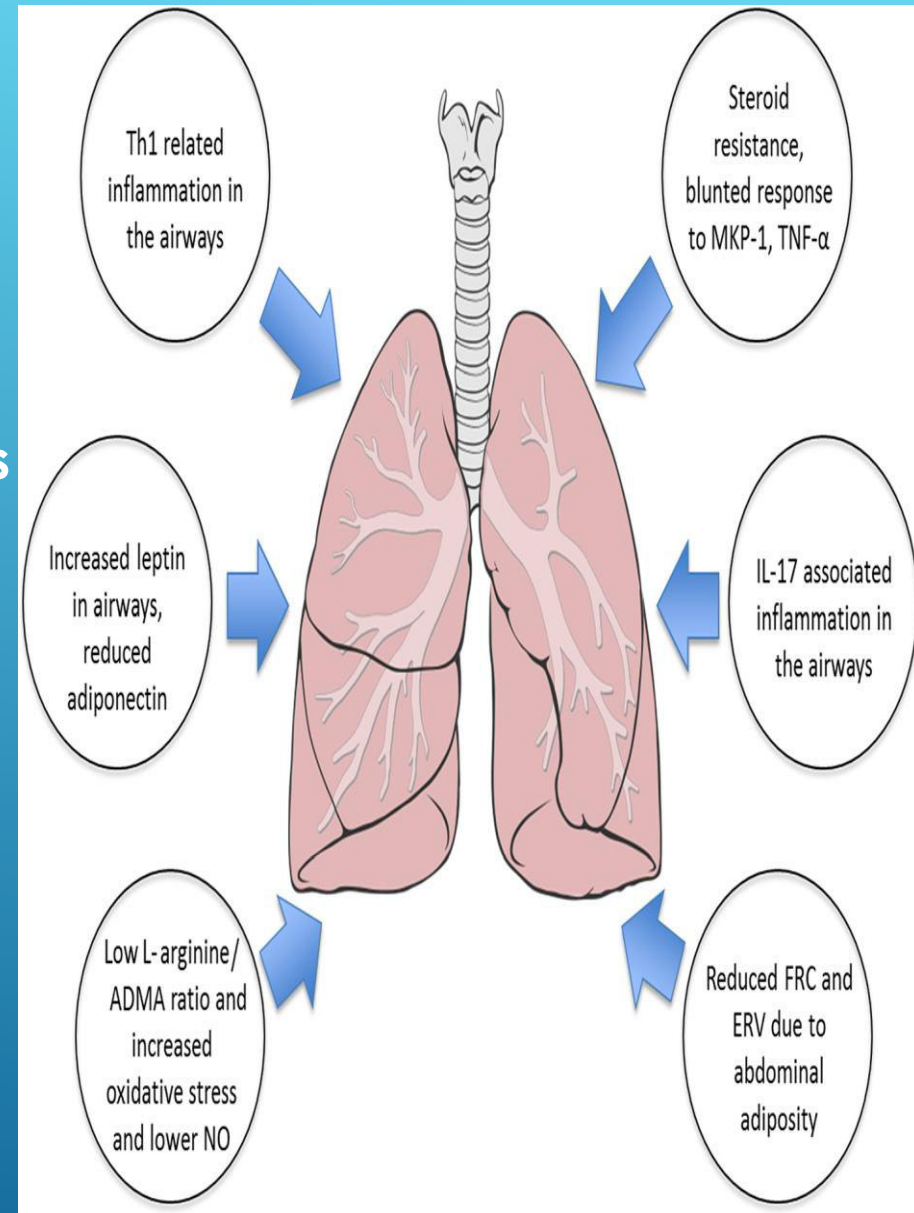
CHILDHOOD OBESITY RELATED ASTHMA

- Th1 polarization ($\text{IFN}\gamma$) vs Th2 (IL-4, IL-5, IL-13, IgE)
- paucity of local airway inflammation
- instead the pathological process is mediated through systemic inflammation.

Murine model studies → part of immunological relationship obesity/asthma may be:

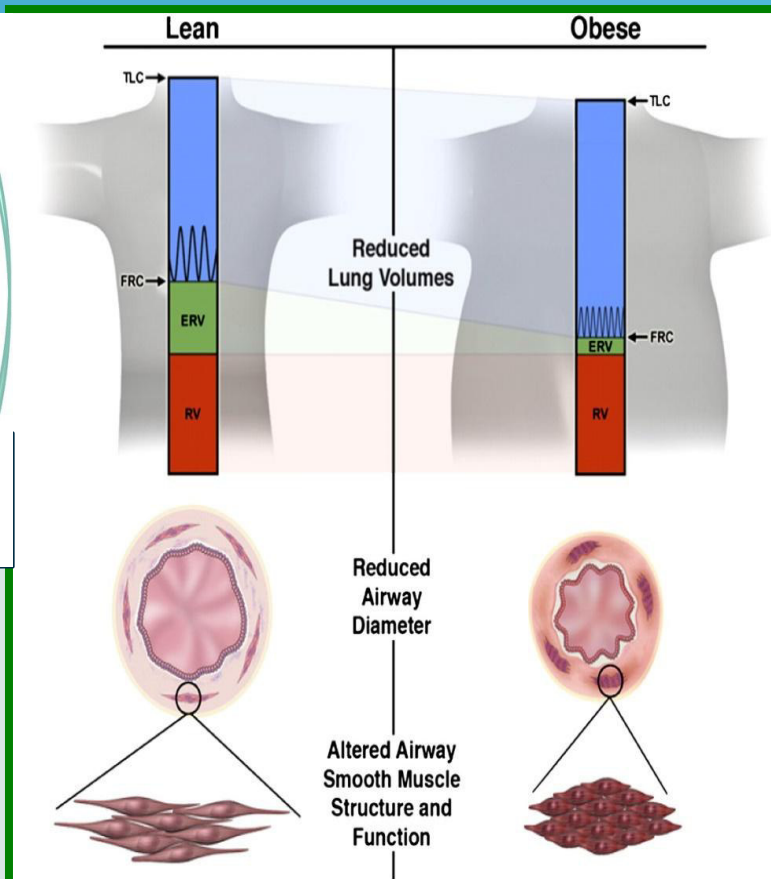
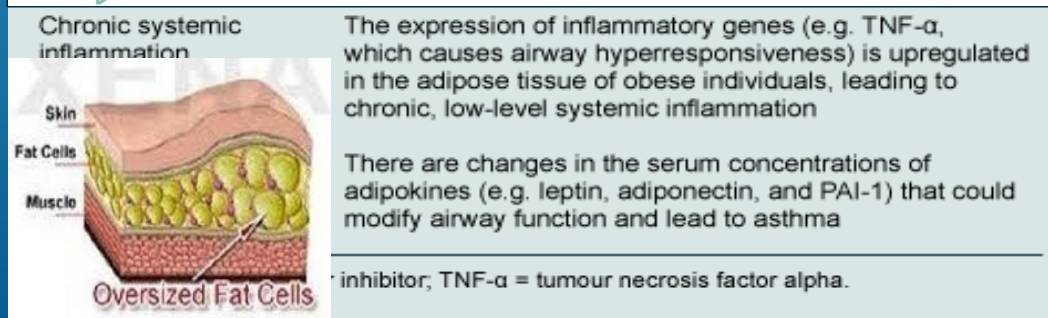
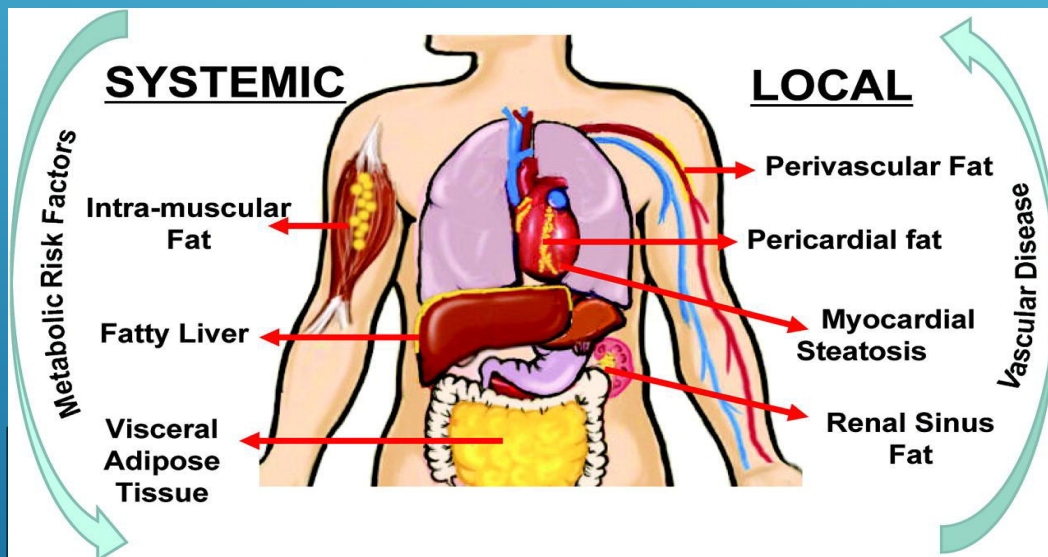
- inflammasome activation
- production of IL-17 cytokine from innate immune cells in the lung.

Obesity related asthma = **part of the systemic inflammation and immune dysregulation** characterizing obesity



L'ANATOMIA DELLE ALTE VIE AEREE dei bambini obesi

- infiltrazione grassa dei muscoli → ne riduce il lume
- depositi grassi nel sottocutaneo → compressione sulle strutture regionali.
- principale ruolo nel bambino = vie aeree più strette
- disturbi respiratori ostruttivi nel sonno (DROS) → OSAS



Un'altra patologia respiratoria correlata all'obesità

Obesity Hypoventilation Syndrome

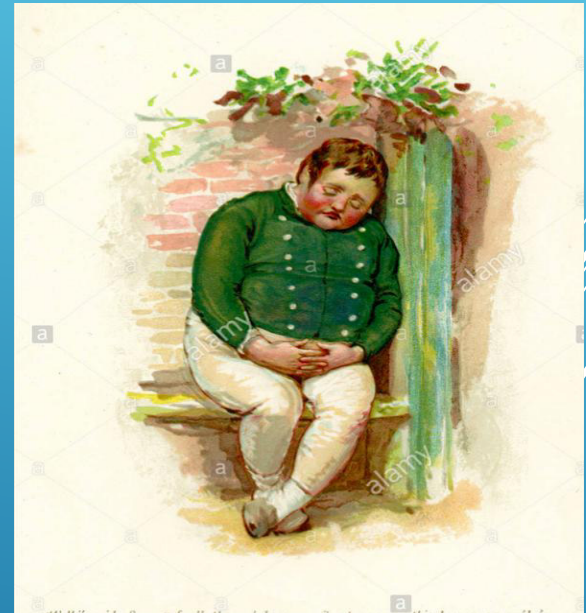
- conosciuta anche come "**Pickwickian Syndrome**"
- l'associazione tra obesità e ipercapnia arteriosa ($\text{PaCO}_2 > 45 \text{ mmHg}$) durante il giorno senza altre cause di ipoventilazione.

CLINICA

- **Ipersonnolenza**
- **stanchezza**
- **cefalea diurna come nelle OSA,**
ma

questi soggetti hanno una

- **ipercapnia**
- **ipossia cronica durante tutto il giorno con policitemia.**
- **evoluzione → ipertens. polmonare cuore polmonare.**
- **durante la notte ipoventilano anche senza OSA.**



VITAMIN D AND ASTHMA

Some studies suggest a role for Vitamin D

Increasing Vitamin D in pregnancy associated with **less wheezing** in offspring

Vitamin D insufficiency in children associated with asthma severity

Serum 25(OH)D levels are inversely associated with recent URTI.

This association may be stronger in those with respiratory tract diseases.

Pediatr Pulmonol 2016 Jun 6. [Epub ahead of print]

Vitamin D & pulmonary function in obese asthmatic children

Lautenbacher LA, Jariwala SP, Markowitz ME, Rastogi D.

We compared % pulmonary function vs. vitamin D categories

→ 72 obese and 71 normal-weight children with asthma

→ serum cytokines associated with Th1 and Th2 inflammation

→ Serum 25-hydroxyvitamin D

RESULTS:

→ Vitamin D deficit in 50% of children not differing by obese status.

→ FEV1 (84.5 vs. 94.8, $P < 0.001$), and FRC (67.5 vs. 79.3, $P = 0.01$) were $<$ in vit D deficient obese asthmatics vs. their sufficient counterparts,

→ TLC was $<$ their vit D insufficient counterparts (86.9 vs. 96.6, $P = 0.01$);

→ similar associations were not observed in NW asthmatics and were not influenced by systemic inflammation.

→ No association between Th1 and Th2 inflammatory measures, vitamin D deficiency, and pulmonary function tests was found.

CONCLUSIONS:

**Vitamin D deficiency associated with pulmonary function deficits among obese children, but not among normal-weight children with asthma, an association that was independent of Th1 and Th2 serum markers
Vit D def= potential mechanism underlying the obese asthma phenotype**



QOL of Life and Health Outcomes in OW and Non-OW Children With Asthma.

Manion AB, Velsor-Friedrich B.



METHODS:

OW and NW 9- to 14-year-olds with asthma.

Health outcomes examined included

- asthma-related missed number of school days,
- emergency department (ED) visits,
- hospitalizations,
- number of days wheezing,
- number of night awakenings.
- QOL was measured using the Pediatric Asthma Quality of Life Questionnaire.

RESULTS:

OB group highest percentage of ED visits, hospitalizations, and number of days wheezing compared with the NW group.

Asthma severity was a significant predictor of overall QOL ($p = .002$).

CONCLUSIONS: obesity = potentially modifiable risk factor for asthma mitigation and prevention.

A Multifactorial Weight Reduction Programme for Children with Overweight + Asthma: a RCT

Willeboordse M, Kant KD, Tan FE

OBJECTIVE:

To determine the effects of weight reduction intervention on asthma management in overweight/obese children with (a high risk of → asthma

RESULTS:

After 18 mos, the BMI-standard deviation score decreased by -0.14 ± 0.29 points ($p < 0.01$) in the intervention group and -0.12 ± 0.34 points ($p < 0.01$) in the control group. This change over time did not differ between groups ($p > 0.05$).

Asthma features (including asthma control and asthma-related quality of life) and lung function indices (static and dynamic) improved significantly over time in both groups.

The Forced Ventilatory Capacity improved especially in the intervention group
- $10.1 \pm 8.7\%$ in the intervention group ($p < 0.001$)
- $6.1 \pm 8.4\%$ in the control group ($p < 0.05$).

CONCLUSIONS & CLINICAL RELEVANCE:

→ some effects were more pronounced in the intervention group (FVC, asthma control, QOL)

Riepilogando

Obesità è un fattore di rischio indipendente per **l'asma piu' severa**, ma non tutti i bambini obesi sviluppano l'asma.

Ruolo di

- dieta, vitamina D
- stile di vita sedentario
- infiltrazione grassa dei muscoli, depositi grasso sottocutaneo
- disregolazione Th1-Th2
- adipokine e infiammazione adiposità-mediata

Miglioramento con la perdita di peso e stile vita

Diagnosi precoce → obesità centrale e circonferenza collo