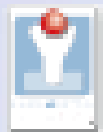


# COMPLICANZE ED EFFETTI COLLATERALI DEI FARMACI

**Silvio Maringhini**  
**U.O.C. Nefrologia Pediatrica**  
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**I.S.M.E.P. A.R.N.A.S. Civico Palermo**



**Fondazione La Nuova Speranza**  
lotta alla glomerulosclerosi focale



**VII INCONTRO NAZIONALE MEDICI  
FAMIGLIE**

**GIARDINI-NAXOS  
23 E 24 APRILE 2017**

# **COMPLICANZE ED EFFETTI COLLATERALI DEI FARMACI**

## **CONCLUSIONI**

**Le complicanze della sindrome nefrosica  
interessano molti organi ed apparati**

**I farmaci usati hanno ridotto le complicanze  
ma hanno effetti collaterali**

**Alternare i farmaci può ridurre la comparsa di  
effetti collaterali irreversibili**

# **COMPLICANZE DELLA SINDROME NEFROSICA**

**Complicanze della malattia**

**Complicanze della terapia**

# **ALTERAZIONI METABOLICHE NELLA SINDROME NEFROSICA**

**Proteinuria ed Ipoalbuminemia**

**Ritenzione idrica**

**Alterazioni elettroliti sierici**

**Iperlipemia**

**Ipercoagulabilità del sangue**

**Ipogammaglobulinemia**

**Ipovitaminosi D**

**Ipotiroidismo**

# COMPLICANZE DELLA SINDROME NEFROSICA

## Complicanze della malattia

**Infettive:** peritonite, cellulite, varicella

**Cardiovascolari:** ipertensione, iperlipemia, coronaropatia

**Respiratorie:** versamento pleurico, embolia

**Ematologiche:** trombosi, anemia

**Gastrointestinali:** intussuscezione

**Renali:** insufficienza renale acuta, trombosi venosa

**Endocrinologiche:** ipotiroidismo, ipodensità ossea

**Neurologiche:** trombosi venosa centrale

# **Polmonite da *Mycoplasma pneumoniae* (MP) nella sindrome nefrosica (SN)**

**Nefrologia, Osp. dei Bambini, Palermo**

**Bambini con SN e sintomi respiratori  
52/124 (42%)**

**Bambini con SN ed infezione da MP  
33/124 (27%)**

**Bambini con SN e polmonite da MP  
14/124 (11%)**

# **INFEZIONI IN CORSO DI SINDROME NEFROSICA IN ETA' PEDIATRICA**

**Nei bambini affetti da sindrome nefrosica:**

- Le infezioni delle vie respiratorie sono frequenti**
- Il *Mycoplasma pneumoniae* è un agente eziologico molto frequente**
- Le infezioni da *Mycoplasma pneumoniae* provocano spesso polmoniti atipiche (paucisintomatiche)**

# Lipoprotein(a) levels in relation to albumin concentration in childhood nephrotic syndrome

DAVIDE NOTO, CARLO M. BARBAGALLO, ARMIDA LO CASCIO, ANGELO B. CEFALÙ, GIOVANNI CAVERA, ROSALIA CALDARELLA, GIUSEPPINA MARINO, SALVATORE TRAVALI, IGNAZIO CUTAIA, SILVIO MARINGHINI, ALBERTO NOTARBARTOLO, and MAURIZIO AVERNA

*Kidney International, Vol. 55 (1999), pp. 2433–2439*

**Table 1.** Clinical and biochemical parameters of 84 children with nephrotic syndrome according to the clinical stage of the disease

	Complete remission	Partial remission	Active disease	P (ANOVA)
Observations	111	51	72	—
Age years	8.1 ± 4.6	8.2 ± 4.3	8.0 ± 4.2	NS
BMI kg/m <sup>2</sup>	19.1 ± 3.5	18.8 ± 3.0	18.8 ± 3.1	NS
P/C <sub>cr</sub> ratio <sup>a</sup>	0.05 (0.06–0.14)	0.6 (0.2–1.84) <sup>c</sup>	7.2 (2.0–246) <sup>ad</sup>	< 0.0001
Albumin g/liter	41 ± 5.0	36 ± 6.2 <sup>c</sup>	27 ± 8.4 <sup>ad</sup>	< 0.0001
TC mmol/liter	4.77 ± 1.64	5.88 ± 1.85 <sup>c</sup>	7.24 ± 2.83 <sup>ad</sup>	< 0.0001
TG mmol/liter	0.99 ± 0.50	1.26 ± 0.57 <sup>c</sup>	1.69 ± 0.82 <sup>ad</sup>	< 0.0001
HDL-C mmol/liter	1.29 ± 0.41	1.42 ± 0.51	1.37 ± 0.51	NS
LDL-C mmol/liter	2.83 ± 1.34	3.63 ± 1.52 <sup>c</sup>	4.77 ± 2.81 <sup>ad</sup>	< 0.0001
ApoA1 g/liter	1.5 ± 0.34	1.63 ± 0.35	1.78 ± 0.42 <sup>c</sup>	< 0.0001
ApoB g/liter	0.93 ± 0.43	1.16 ± 0.43 <sup>c</sup>	1.50 ± 0.68 <sup>ad</sup>	< 0.0001
Lp(a) <sup>ab</sup> mg/dl	11.0 (0.4–206)	16.4 (1–153)	18.4 (0.5–222) <sup>c</sup>	0.038

Definitions are: complete remission, P/C<sub>cr</sub> ratio < 0.2; partial remission, P/C<sub>cr</sub> ratio > 0.2 and < 2.0; active disease: P/C<sub>cr</sub> ratio > 2.0 (see **Methods** section for details). Student's *t*-test for independent data was used for this analysis. Abbreviations are in the **Appendix**.

<sup>a</sup>After log transformation; range in brackets

<sup>b</sup>Adjusted for apo(a) isoform distribution (see **Statistics** Section)

<sup>c</sup>*P* < 0.05 vs. Complete remission

<sup>d</sup>*P* < 0.05 vs. Partial remission

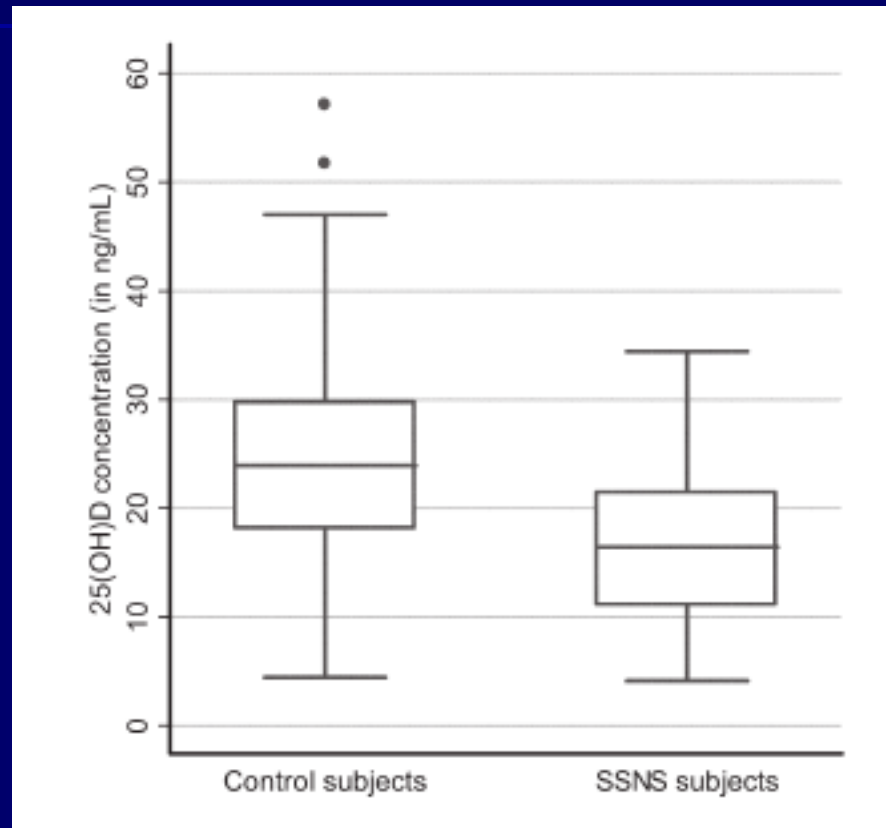


# COMPLICANZE TROMBOEMBOLICHE NELLA SINDROME NEFROSICA

Table. 2 Frequency of clinically apparent TEC in children with NS

Authors	No of children with TEC	%
Our data	9/447	2.0
Andrew and Brooker 1996 [10]	139/4,158	3.3
Egli et al. 1973 [11]	64/3,377	1.8
Mehls et al. 1987 [12]	9/204	4.4

# CARENZA DI VITAMINA D NELLA SINDROME NEFROSICA



# COMPLICANZE DELLA SINDROME NEFROSICA

## Complicanze della terapia

**Corticosteroidi:** cataratta, bassa  
statura, alterazioni ossee, eretismo psichico

**Levamisolo:** vasculite, leucopenia

**Agenti alchilanti:** sterilità, neoplasie, cistite  
emorragica, alopecia

**Inibitori della calcineurina:** iperplasia gengivale,  
irsutismo, ipertensione, nefrotossicità

**Micofenolato:** vomito, diarrea, leucopenia

**Rituximab:** neutropenia, infezioni, polmonite  
interstiziale, encefalopatia, miocardite

# COMPLICANZE A LUNGO TERMINE DELLA SINDROME NEFROSICA INSORTA IN ETA' PEDIATRICA

Hjorten R. et al. *Frontiers in Pediatrics*, 2016

**TABLE 1 | Long-term complications of childhood SSNS.**

	Complication	Reported prevalence
Renal	Relapses in adulthood	5–40% (47, 48)
	Decreased GFR/ESRD	<1% at 20-year follow-up (48)
	Hypertension	6–46% (49, 50)
Immunosuppression-related	Overweight/obesity	8–23% (50, 51)
	Growth failure	8–16% (48, 50)
	Osteoporosis	13–63% (49, 50)
	Fractures	20% (51)
	Cataracts	6–20% (49, 50)
	Infertility	Up to 75–94% (49, 51)
	Malignancy	Unknown
Psychosocial	Educational status and employment	<10% failure to complete high school and <45% unemployed (51)
	Marital status/stable relationships	<40% unmarried or not in stable relationship (51)

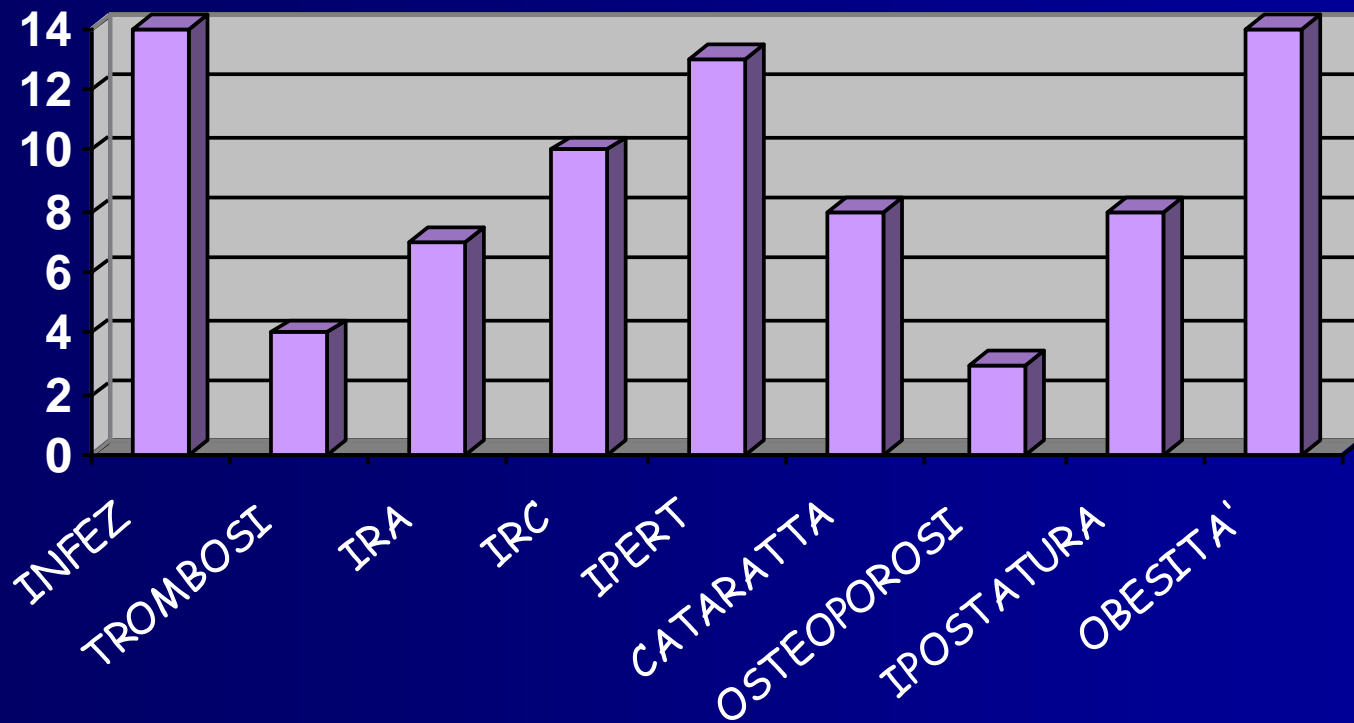
# COMPLICANZE DELLA SINDROME NEFROSICA

U.O.C. Nefrologia Pediatrica  
Ospedale dei Bambini "G. Di  
Cristina"

- 153 bambini affetti da SN (108 M, 45 F)  
afferenti alla nostra U.O. dal 2000 al 2010

# COMPLICANZE DELLA SINDROME NEFROSICA

U.O.C. Nefrologia Pediatrica  
Ospedale dei Bambini "G. Di  
Cristina"



# **COMPLICANZE DELLA SINDROME NEFROSICA**

## **Complicanze della terapia**

### **Corticosteroidi:**

**bassa statura**

**alterazioni ossee**

**cataratta**

*Personal Practice\**

*Arch. Dis. Childh.*, 1968, **43**, 257.

## Management of the Nephrotic Syndrome

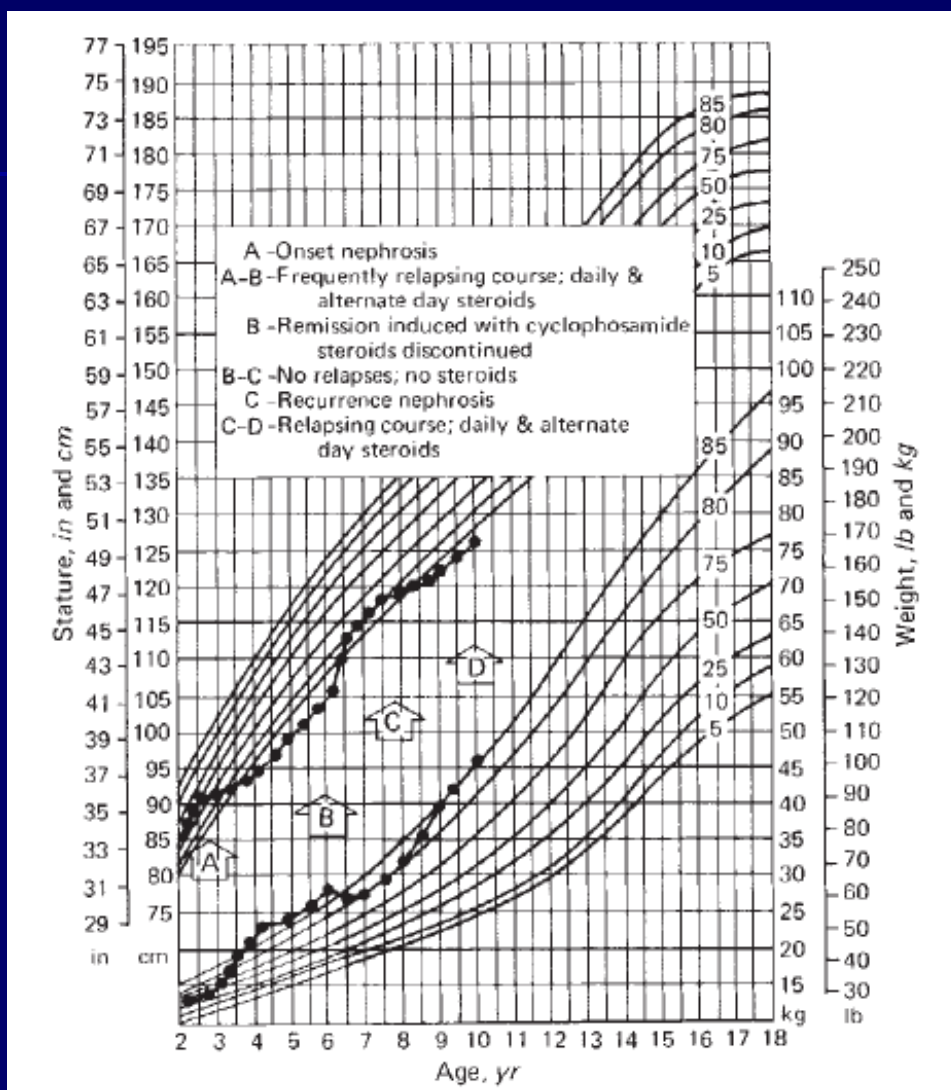
GAVIN C. ARNEIL

*From the Department of Child Health, University of Glasgow*

The **reduction in the mortality** of idiopathic nephrosis is certainly as much due to efficient **antibiotics** as to specific effect of **steroid** therapy.



# CRESCITA STATURALE NELLA SINDROME NEFROSICA



# Growth and endocrine function in steroid sensitive nephrotic syndrome

L REES, S A GREENE, P ADLARD,\* J JONES,\* G B HAYCOCK, S P A RIGDEN, M PREECE,\* AND C CHANTLER

*Archives of Disease in Childhood*, 1988, **63**, 484–490

**Growth** in both boys and girls, **worsened** significantly with chronological age. There was a significant negative correlation between AHT SDS and **duration of treatment** in boys, but not in girls.

**In adolescent boys** treated long term for steroid sensitive nephrotic syndrome corresponded with the clinical picture of **delayed onset of puberty**, which accounted for severe growth retardation in a substantial proportion of subjects.

# CRESCITA STATURALE NELLA SINDROME NEFROSICA

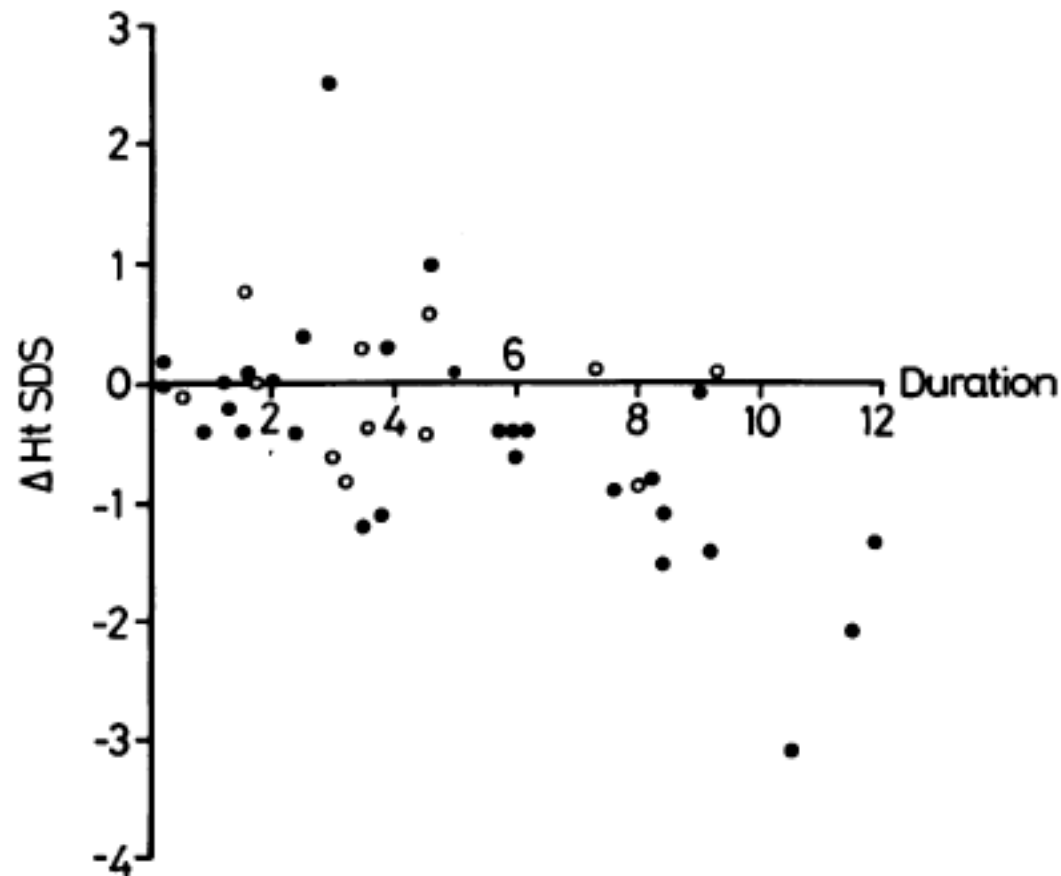


Fig 2 Relation between duration of treatment (in years) and change in height standard deviation score ( $\Delta Ht SDS$ ) in boys (●) and girls (○).

# CRESCITA STATURALE NELLA SINDROME NEFROSICA

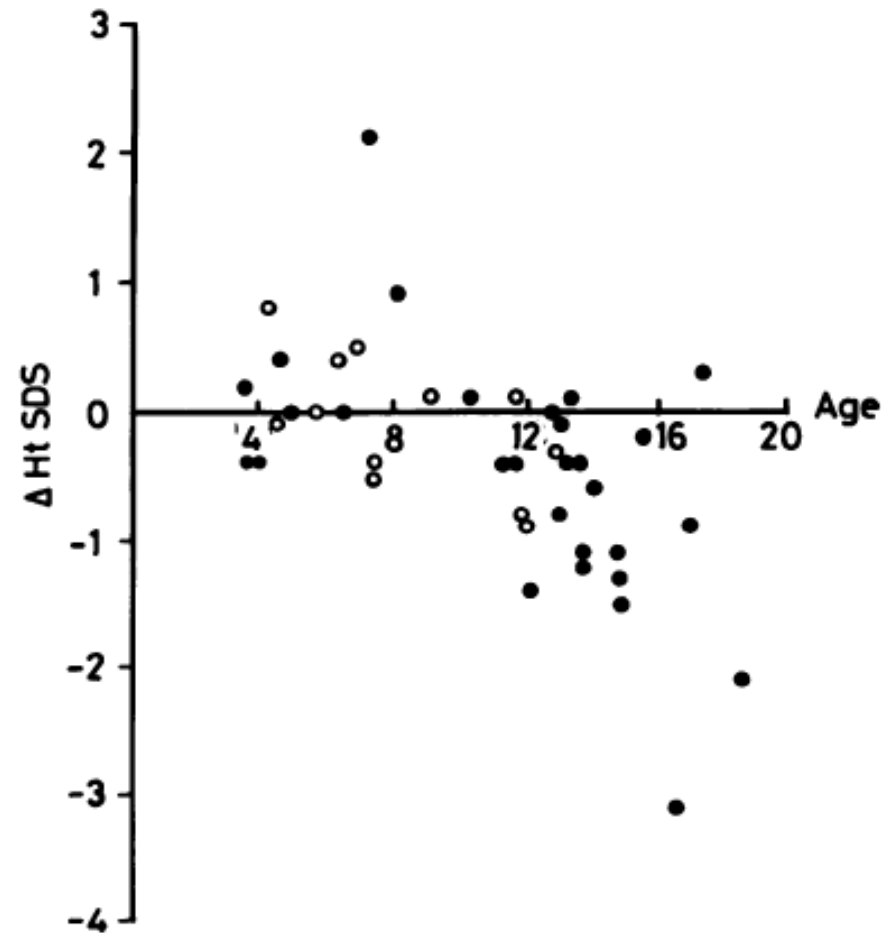


Fig 1 Relation between age (in years) at last examination and change in height standard deviation score ( $\Delta$ Ht SDS) in boys (●) and girls (○).

# The Effect of Long-term Steroid Therapy on Linear Growth of Nephrotic Children

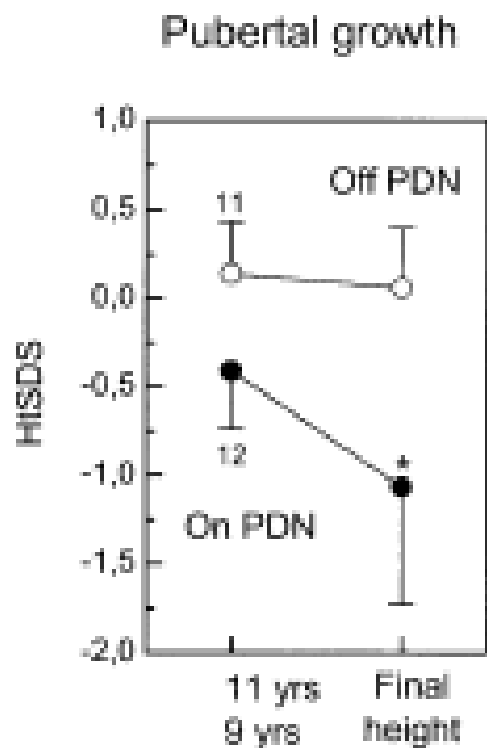
Abbas Madani<sup>1,2</sup>, MD; Sham-una Umar<sup>2</sup>, MD; Rambod Taghaodi<sup>1</sup>, MD; Niloofar Hajizadeh<sup>\*1,2</sup>, MD; Ali Rabbani<sup>1,2</sup>, MD, and Hadi Z-Mehrjardi<sup>3</sup>, MD, MPH

*Iranian Journal of Pediatrics, Volume 21 (Number 1), March 2011, Pages: 21-27*

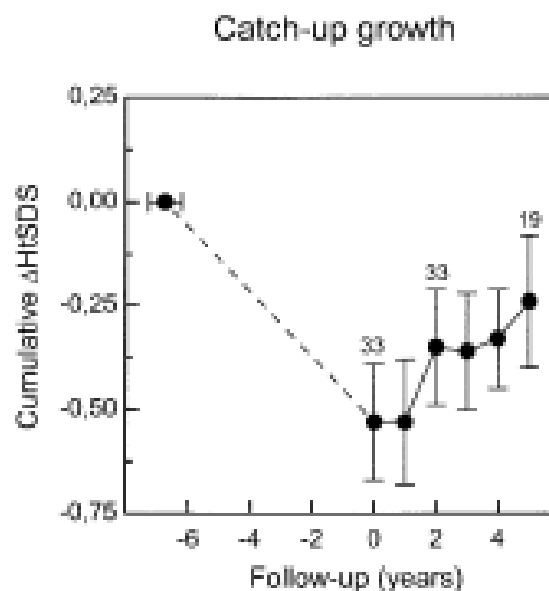
**Conclusion** No statistically significant retardation of linear growth was observed in the study population as a group following treatment with prednisolone according to the guidelines of ISKDC. Although about 62 subjects had growth retardation, children treated with prednisolone were not different from those who had increased growth.

# CRESCITA STATURALE NELLA SINDROME NEFROSICA

B



C



Pediatr Nephrol (2003) 18:783–788

# CATARATTA NELLA SINDROME NEFROSICA

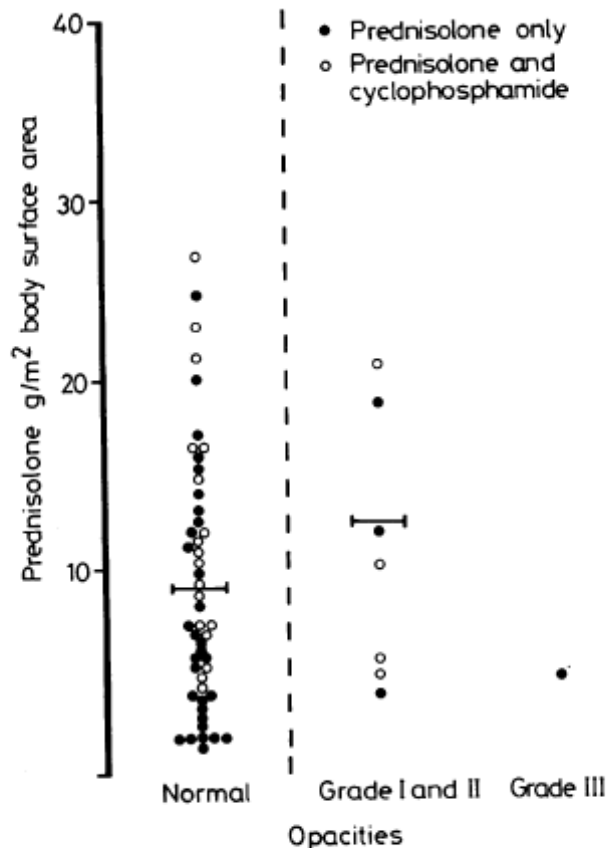


Fig. 2 Effects of total dose of prednisolone treatment on lens opacities.

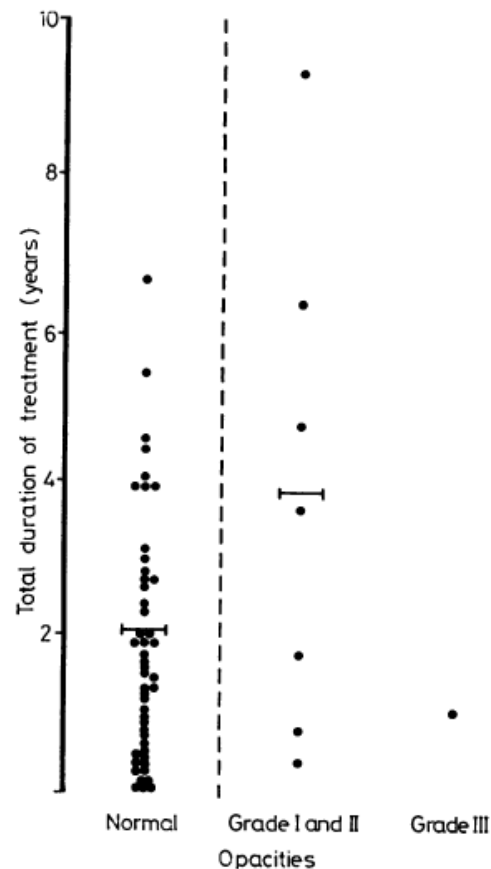


Fig. 3 Effect of total duration of prednisolone treatment on lens opacities.

# Corticosteroid-induced cataracts in idiopathic nephrotic syndrome

J T BROCKLEBANK, R B HARCOURT, AND S R MEADOW

*Archives of Disease in Childhood*, 1982, 53, 30–34

The incidence and severity of posterior subcapsular cataracts were studied in **58 children** with steroid-sensitive nephrotic syndrome. **Eight (14%)** children had cataracts.

**Visual acuity was normal** in all but one child.

there is **little risk of causing permanent visual** handicap in children with steroidsensitive nephrotic syndrome, provided prednisolone treatment is carefully controlled.



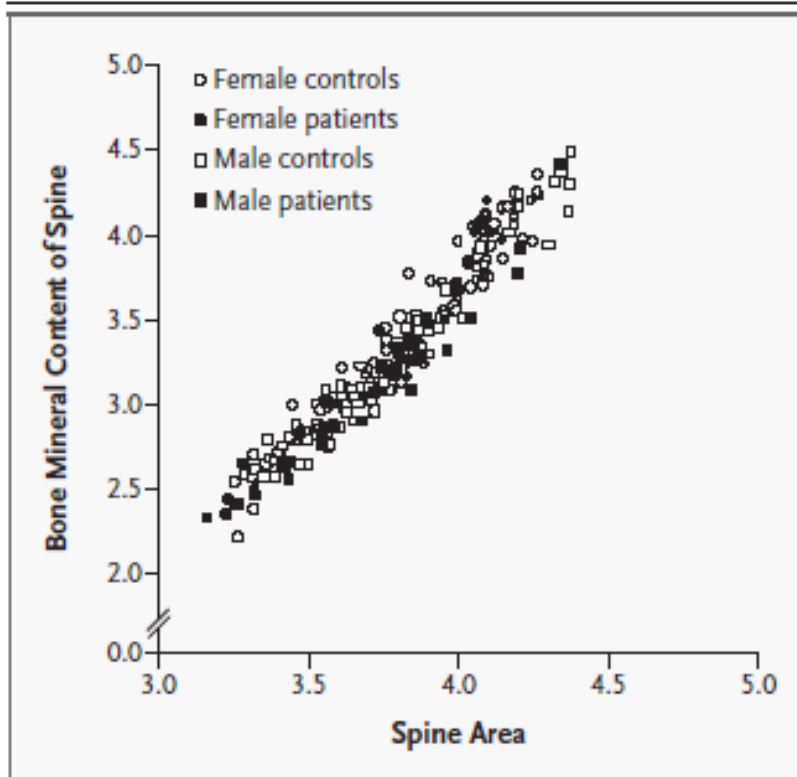
# OSTEODISTROFIA NELLA SINDROME NEFROSICA

## Long-Term, High-Dose Glucocorticoids and Bone Mineral Content in Childhood Glucocorticoid-Sensitive Nephrotic Syndrome

Mary B. Leonard, M.D., M.S.C.E., Harold I. Feldman, M.D., M.S.C.E.,  
Justine Shults, Ph.D., Babette S. Zemel, Ph.D., Bethany J. Fost N Engl J Med 2004;351:868-75.  
and Virginia A. Stallings, M.D.

**Intermittent treatment** with high-dose glucocorticoids during growth **does not** appear to be associated with **deficits in the bone mineral content** of the spine or whole body relative to age, bone size, sex, and degree of maturation.

# OSTEODISTROFIA NELLA SINDROME NEFROSICA



**Figure 1.** Bone Mineral Content of the Lumbar Spine Relative to Bone Area in Patients with Glucocorticoid-Sensitive Nephrotic Syndrome and Control Subjects. Values have been log-transformed.

# **COMPLICANZE DELLA SINDROME NEFROSICA**

## **Complicanze della terapia**

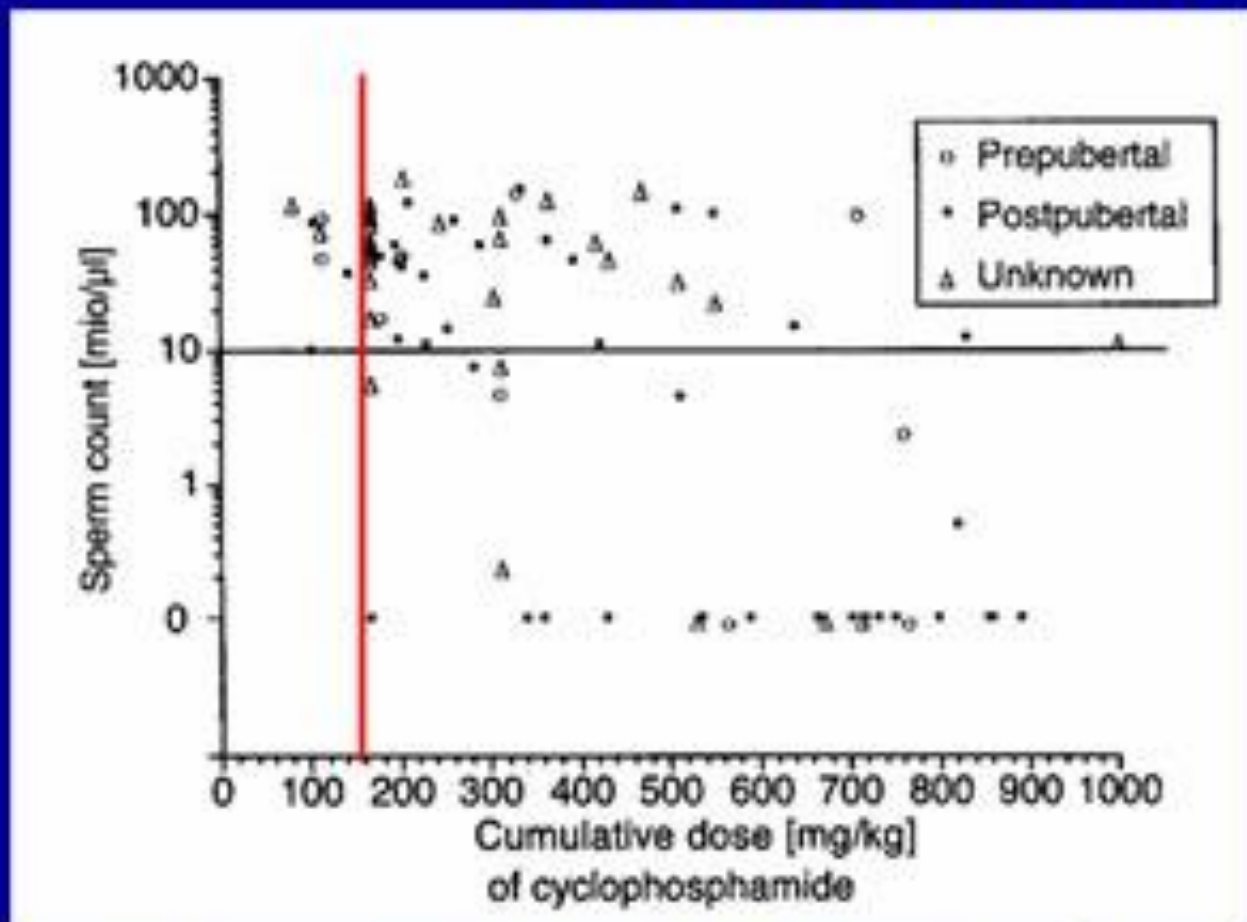
### **Agenti alchilanti:**

**sterilità**

**neoplasie**

# Cyclophosphamide and male fertility

Latta *et al* *Pediatr Nephrol* 2001 16 271-282



- Data pooled from 8 studies (119 patients)
- Dose dependent effect on sperm count

# Hodgkin Lymphoma and Nephrotic Syndrome in Childhood

Piero Farruggia, Antonino Trizzino, Silvio Maringhini, Antonella Grigoli, Chiara Sapia, Mariella D'Alessandro, Serena Tropa, Paolo D'Angelo

The Indian Journal of Pediatrics. 2010, 77, 10, 1147–1149

... the incidence of nephrotic syndrome in Hodgkin lymphoma is less than **1%** ....there are about **50 pediatric cases** published, no one among Italian children.  
In the present paper, the authors report **2 cases** observed in 7 yrs period.



# Malignancy

Latta et al *Pediatr Nephrol* 2001 16 271-282

- 2/866 following cyclophosphamide (0.2%)
- 3/534 following chlorambucil (0.6%)
- Prevalence of paediatric malignancy in UK  
1/600 by 15th birthday (0.17%)

# **COMPLICANZE DELLA SINDROME NEFROSICA**

**Complicanze della terapia**

**Inibitori della calcineurina:**

**nefrotossicità**

# Risk Factors for Cyclosporin A Nephrotoxicity in Children with Steroid-Dependant Nephrotic Syndrome

Severin Kengne-Wafo,\* Laura Massella,\* Francesca Diomedi-Camassei,<sup>†</sup>  
Alessandra Gianviti,\* Marina Vivarelli,\* Marcella Greco,\* Gilda Rita Stringini,\* and  
Francesco Emma\*

*Clin J Am Soc Nephrol* 4: 1409–1416, 2009.

