

ORIGINAL ARTICLE

Bone mineral density in children with moderate to severe atopic dermatitis

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Background: Low bone mineral density (BMD) has been reported in 30.4% of adult patients with atopic dermatitis (AD).

Objective: The aim of this study was to determine the prevalence of low BMD in children with moderate to severe AD and to investigate the relation between BMD and corticosteroid and cyclosporine therapy.

Methods: Lumbar spine BMD was measured by dual-energy X-ray absorptiometry in 60 children (age 5-16 years) with moderate to severe AD. BMD (in g/cm²) was expressed in Z-scores, the number of SD above or below the mean value of an age- and sex-matched reference population. In children, low BMD was defined as a Z-score less than -2. Information on lifestyle parameters and bone fractures were collected by use of a standardized questionnaire. The cumulative dose of corticosteroids and cyclosporine therapy was calculated for the previous 5-year period.

Results: Three patients (5%) had low BMD; one patient (1.7%) had osteoporosis. The observed prevalence of low BMD in this study (6.7%; 95% confidence interval 1.8%-16.2%) does not differ from the expected prevalence of low BMD in the general population ($P = .06$). Overall, use of topical corticosteroids in the previous 5 years was not associated with a decrease in BMD (Z-score). When children received additional systemic treatment (oral corticosteroids and/or cyclosporine) in the previous 5 years, BMD decreased, although the decrease was not statistically significant. Correction for lifestyle parameters did not change these associations.

Limitations: The number of patients studied was limited. The cumulative dose of corticosteroids and cyclosporine therapy was only registered for the previous 5 years, and relatively low amounts of topical corticosteroids were used. The definition of low BMD differs between adults (Z-score < -1) and children (Z-score < -2). Because there is no Dutch BMD reference population for children, normative BMD references were obtained from a different population (US children).

Conclusions: Low BMD did not occur more frequently in this population of children with moderate to severe AD compared with the general population. Use of topical corticosteroids in the previous 5 years was not associated with a decrease in BMD. (J Am Acad Dermatol 10.1016/j.jaad.2009.12.015.)

Key words: atopic dermatitis; bone mineral density; children; cyclosporine; topical corticosteroids.

Atopic dermatitis (AD) is a common inflammatory skin disease in children worldwide, with a variable prevalence of 12% to 37%.¹ Topical corticosteroids represent the mainstay of

treatment, but there is widespread concern about adverse effects. Systemic use of corticosteroids in children is associated with a decrease in bone mineral density (BMD) and bone turnover.^{2,3} Topically

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applied corticosteroids can also exert a systemic effect through percutaneous absorption.^{4,5} Recently, a high incidence (30.4%) of low BMD (Z-score < -1) was described in adult patients with moderate to severe AD.⁶

During childhood and adolescence, BMD increases until peak bone mass is reached at approximately 21 years of age.⁷ Achieving a normal peak bone mass is important in the prevention of low BMD and osteoporosis later in life. Pedreira et al⁸ did not find an association between the use of topical corticosteroids and a decreased BMD in children with moderate to severe AD although decreased BMD in children using cyclosporine was observed. These authors did not define low BMD by Z-scores and presented the absolute decrease in BMD. Because the definition of low BMD in children is based on Z-scores,⁹ it cannot be concluded that an absolute decrease in BMD is of clinical relevance.

Factors other than topical or oral medication may put children with moderate to severe AD at risk for low BMD. Treatment of coexisting atopic diseases must be considered because up to 33% of the children with AD have asthma or allergic rhinitis¹⁰ and may use inhalation/nasal corticosteroids. Up to 30% of children with AD can have intolerance or allergy to cow's milk at some point in their lives¹¹ and calcium intake could be insufficient. Furthermore, AD has the potential to interfere with physical activity.¹² The aim of this study was to investigate the frequency of low BMD (Z-score < -2) and its association with AD therapy (topical corticosteroids, oral corticosteroids, cyclosporine), AD-associated therapy (inhalation corticosteroids), and lifestyle parameters (dairy intake, physical activity) in children with moderate to severe AD.

METHODS

Patients

In this cross-sectional study 60 children with moderate to severe AD were included between January 2008 and February 2009. All patients were aged between 5 and 16 years. The diagnosis of AD was made according to the criteria of Hanifin and Rajka.¹³ All children were currently treated at the outpatient department of pediatric

dermatology/allergology of our institution. Children were included if one of the following criteria was present: objective scoring AD (SCORAD) index greater than 20; more than 4 visits to the outpatient department in 1 year; history of a hospital admission for the treatment of AD; or current use of potent topical corticosteroids (class III) or history or current use of systemic immunosuppressive treatment (prednisone and/or cyclosporine). Children with comorbidity such as renal diseases, rheumatoid arthritis, inflammatory bowel disease, cystic fibrosis, endocrinologic disorders, or bone diseases were excluded. The local medical ethical committee approved this study and patients and/or their parents or caregivers gave their written informed consent.

Questionnaire

All patients were interviewed with the help of their parents by use of a structured questionnaire. Participants were asked if they experienced or had experienced allergic asthma, allergic rhinitis, or cow's milk allergy. The amount of daily dairy intake (cow's milk, yogurt, or cheese), the level of general physical activity (ie, sports attendance), and daily exposure to sunlight was determined. Subsequently, the total number of years patients were treated for AD was recorded.

Corticosteroid and cyclosporine use

Cumulative dose of topical, inhaled, and systemic corticosteroids and topical tacrolimus and pimecrolimus was calculated for 5 years before the visit to our clinic. This was carried out using the pharmacy records of each patient as previously described by Haeck et al.⁶ Use of cyclosporine was recorded for the last 5 years. The total number of years of AD therapy was determined from the patients' history.

Cumulative topical and inhalation/nasal corticosteroids were divided into 3 groups according to the amount used in the previous 5 years. Topical corticosteroid use was graded as low (<30 g/mo), medium (30-50 g/mo), or high (>50 g/mo). Use of inhalation/nasal, oral corticosteroids and cyclosporine was categorized into two groups: use or no use in the previous 5 years. In this way 4 different risk groups were determined (Table I).

CAPSULE SUMMARY

- Corticosteroids and/or cyclosporine therapy may put children at risk for development of low bone mineral density.
- In this population of children with moderate to severe atopic dermatitis the use of topical/inhalation/oral corticosteroids or cyclosporine was not associated with a significant decrease in bone mineral density.
- We found no evidence that low bone mineral density occurs more frequently in children with atopic dermatitis compared with the general population.

Abbreviations used:

AD:	atopic dermatitis
BMD:	bone mineral density
DXA:	dual-energy X-ray absorptiometry
25-OH-vitamin D:	25-hydroxyvitamin D
PTH:	parathyroid hormone
SCORAD:	scoring atopic dermatitis

BMD measurement; dual-energy X-ray absorptiometry scan

BMD was measured by dual-energy X-ray absorptiometry (DXA), using the Hologic QDR-4500 Discovery A (software version 12.3, Hologic Inc, Bedford, MA) X-ray bone densitometer. The manufacturer specified coefficient of variation is 1% (calculated: $100 \times \text{SD}/\text{mean}$). The SD for the lumbar spine BMD is 0.00806 g/cm^2 . Daily quality assurance was performed, and all children were assessed by the same analyst. Before the BMD measurement, height and weight of the children was measured. Then, BMD was measured in the lumbar vertebrae L1 to L4. Data are expressed as Z-scores, the number of SD above or below the mean value of an age- and sex-matched reference population. Because BMD in DXA is dependent of bone size, and a larger bone size may artificially inflate BMD,¹⁴ correcting Z-score for body height is necessary to prevent incorrect diagnosis of osteoporosis in children with a small body size for their age.¹⁵ Children with AD can have small body height as a result of chronic inflammation^{16,17} and we corrected all analysis for body height (age adjusted). Reference data for healthy Dutch children are not available for the bone densitometer (Hologic Inc).¹⁸ The pediatric reference database incorporated in the software was used. This reference population consists of age- and sex-specific BMD reference values from more than 1400 Caucasian children in the United States.¹⁹ According to the International Society for Clinical Densitometry recommendations⁹ osteoporosis was defined as a Z-score less than -2 with a fracture history. Low BMD was defined as a Z-score less than -2 without a significant fracture history. The DXA scans were reported by nuclear medicine physicians who were aware of the patients' diagnosis, but not of the treatment history.

Disease activity

Disease activity was recorded on the same day as the BMD measurement was performed, and was scored using the objective SCORAD index.²⁰ In addition the level of serum thymus and activation-regulated cytokine was measured as an objective

Table 1. Definition of risk groups

	Risk (+)
Group 1	Medium/high topical corticosteroid use + inhalation corticosteroid use
Group 2	Medium/high topical corticosteroid use + inhalation corticosteroid use + oral corticosteroid use
Group 3	Medium/high topical corticosteroid use + inhalation corticosteroid use + cyclosporine use
Group 4	Medium/high topical corticosteroid use + inhalation corticosteroid use + oral corticosteroid use + cyclosporine use

Children were assigned to a risk group if all of above criteria were present.

marker for disease activity.^{21,22} Thymus and activation-regulated cytokine reference levels are 0 to 100 pmol/L.

Biochemical parameters

Plasma concentrations of parathyroid hormone (PTH) and serum concentrations of calcium, albumin, phosphate, and 25-hydroxyvitamin D (25-OH-vitamin D) were measured. Vitamin D deficiency was defined as a serum 25-OH-vitamin D level of less than 50 nmol/L and vitamin D insufficiency was defined when levels were between 51 and 74 nmol/L.²³

Statistical analysis

Statistical analysis was performed using a software program (SPSS for Windows, Version 15.0, SPSS Inc, Chicago, IL). Data were expressed as frequencies (number of patients or percentages) for categorical variables and as a mean $\pm$ SD for continuous variables. The children's height and weight were expressed by age- and sex-adjusted Z-scores.

To investigate whether the expected versus observed percentage of children with a low BMD differed significantly the binominal test was done (test proportion set on 2.5%).

The association between topical corticosteroid use and lumbar spine Z-score was investigated by use of univariate and multivariate linear regression. Topical corticosteroid use was expressed as a continuous variable and as a categorical variable. The association among the 4 risk groups and lumbar spine Z-score was determined. Multivariate linear regression was done to adjust for length Z-score, weight Z-score, dairy intake, and physical exercise as these are potential confounders.

The correlation between the number of fractures and lumbar spine Z-score was determined using the

Spearman rho test, because the number of fractures had a skewed distribution. Differences in the number of fractures in risk groups 1 to 4 were determined by use of the Mann-Whitney test. Finally, we compared Z-scores among normal, deficient, and insufficient levels of 25-OH-vitamin D.

RESULTS

Baseline characteristics of study population

Baseline characteristics are presented in Table II. Sixty children, 24 boys and 36 girls, age 5 to 16 years, with moderate to severe AD were included. At the moment of inclusion patients had active skin disease, indicated by a mean objective SCORAD of 31 ± 14 ($\pm$ SD) and a median serum thymus and activation-regulated cytokine of 945 (interquartile range: 457-1895) pmol/L. Patients had received treatment for 1.5 to 16.2 (median 7.7) years. All patients used topical corticosteroids to control their skin disease at the moment of inclusion; most frequently class III topical corticosteroids (class IV being the most potent) were used. Total cumulative use (class I-IV) of topical corticosteroids in the previous 5 years ($\pm$ SD) was 2044 ± 1838 g. In addition, 25% of the patients required treatment with one or more courses of oral corticosteroids and 13.3% were treated with cyclosporine in the previous 5 years. Furthermore, 53.3% were given a diagnosis of asthma/allergic rhinitis and used inhalation/nasal corticosteroids and 53.4% had cow's milk allergy (currently or in the past). Dairy intake and physical activity were low in 71.1% and 13.3%, respectively.

Bone mineral density

Three patients (5%) were given a diagnosis of low BMD (Z-score < -2 in lumbar spine), and one patient (1.7%) was given a diagnosis of osteoporosis (Z-score < -2 and a significant fracture history) (Table II). All 3 patients with low BMD had used topical corticosteroids for at least 10 years. None of these patients had previously used oral corticosteroids or cyclosporine. One patient also used inhalation corticosteroids and his dairy intake and physical activity were inadequate. Topical corticosteroid use was low in two patients with a cumulative use of 555 and 575 g, respectively, and high in one patient with use of 2990 g in 5 years. Disease activity at the moment of inclusion was high with an objective SCORAD of 24, 33, and 45. One patient reported a bone fracture after trauma. No significant family history of fractures was present.

The patient with osteoporosis (age 6 years) had not previously used inhaled/oral corticosteroids or cyclosporine. Topical corticosteroids were applied

Table II. Baseline characteristics of patients with atopic dermatitis (n = 60)

No. of patients with AD	60
Sex	
Male	24 (40%)
Female	36 (60%)
Mean age, y $\pm$ SD	10.5 ± 3.4
Length Z-score, mean $\pm$ SD	-0.17 ± 1.14
BMD lumbar spine Z-score*, No. of patients	
Normal	56 (93.3%)
Diminished	3 (5%)
Osteoporosis	1 (1.7%)
Cumulative dose of topical corticosteroids, mean g $\pm$ SD [†]	
Class I	47 ± 96
Class II	385 ± 806
Class III	1558 ± 1405
Class IV	56 ± 134
Total all classes	2044 ± 1838
Cumulative dose of topical tacrolimus or pimecrolimus, median g (IQR)	120 (30-330)
Use of oral corticosteroids, No. of patients	15 (25%)
Cumulative dose of oral corticosteroids, mean mg $\pm$ SD [†]	559 ± 406
Use of inhalation corticosteroids, No. of patients	32 (53.3%)
Cumulative dose of inhalation corticosteroids, mean mg $\pm$ SD [†]	326 ± 294
Use of cyclosporine, No. of patients	8 (13.3%)
Duration of cyclosporine therapy, mean mo $\pm$ SD [†]	11 ± 5
Duration of AD treatment, mean y $\pm$ SD	8.1 ± 3.8
Disease activity	
Objective SCORAD, mean score $\pm$ SD	30 ± 12
SA-EASI, mean score $\pm$ SD	15 ± 12
TARC, median pmol/L (IQR)	945 (459-1895)
Dairy intake, No. of patients [‡]	
<4 U/d (low)	43 (71.7%)
>4 U/d (normal)	17 (29.3%)
Physical exercise, No. of patients	
>2 times weekly (high)	25 (41.7%)
1-2 times weekly (normal)	27 (45.0%)
<1 time weekly (low)	8 (13.3%)
Fractures, No. of patients	
None	45 (75%)
≥ 1	15 (25%)

AD, Atopic dermatitis; BMD, bone mineral density; IQR, interquartile range; SA-EASI, Self-administered Eczema Area and Severity Index; SCORAD, scoring atopic dermatitis; TARC, thymus and activation-regulated cytokine.

*International Society for Clinical Densitometry criteria: diminished BMD if Z-score -2.0 and osteoporosis if Z-score -2.0 and a significant fracture history.

[†]Use in 5 y before inclusion.

[‡]1 U of dairy = one glass of dairy.

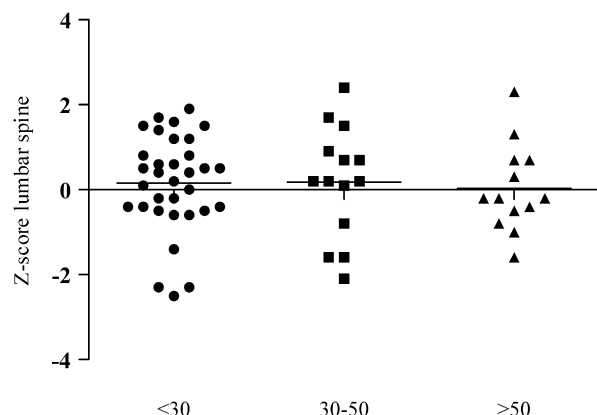


Fig 1. Lumbar spine Z-scores in children with atopic dermatitis ($n = 60$) using different amounts of topical corticosteroids, defined as mean dose in grams per month of all classes of topical corticosteroids used in previous 5 years; $P = .935$.

for 3 years with a cumulative amount of 1230 g. The objective SCORAD at inclusion was 30. Dairy intake and physical activity were within normal limits. The patient reported two arm fractures and one digital fracture after trauma. The younger sister of this patient reported two fractures after trauma; she had no history of AD. This patient was referred to an endocrinologist where no abnormalities in bone-related laboratory parameters were found.

Expected versus observed numbers of patients with low BMD

In a normally distributed population 2.5% (2 of 60 in this study) are expected to have a low BMD (Z-score < -2). The observed percentage of children with a low BMD is 6.7% (4 of 60; 95% confidence interval 1.8%-16.2%) in the study population. The difference between the expected and observed percentage of children with a low BMD is not significant ($P = .06$).

Cumulative dose of topical corticosteroids and BMD

Use of topical corticosteroids was not associated with a lower lumbar spine Z-score (adjusted for height, inhalation/oral corticosteroids, and cyclosporine; $\beta = 0.105$, SE = 0.092, $P = .260$). When topical corticosteroid use was divided into groups with low, medium, and high cumulative use, higher use of topical corticosteroids was not associated with a decrease in lumbar spine Z-score (Fig 1 and Table III). Additional adjustment for weight, physical activity, and dairy intake did not change the association.

Topical corticosteroids, inhalation corticosteroids, oral corticosteroids, cyclosporine, and BMD

Patients using medium or high amounts of topical and inhalation/nasal corticosteroids (risk group 1; $n = 20$) did not have a lower lumbar spine Z-score than patients using low ($n = 40$) amounts of topical and no inhalation corticosteroids ($\beta = 0.294$, SE = 0.291, $P = .316$), when adjusted for height.

However, lumbar spine Z-score decreased with 0.082 when patients had also used oral corticosteroids (risk group 2; $n = 10$; $\beta = -0.082$, SE = 0.37, $P = .825$) and lumbar spine Z-score decreased with 0.303 when patients had also used cyclosporine (risk group 3; $n = 5$; $\beta = -0.303$, SE = 0.50, $P = .549$). Finally, children with additional use of both oral corticosteroids and cyclosporine in the previous 5 years (risk group 4; $n = 3$) had the most prominent decrease in lumbar spine Z-score ($\beta = -0.573$, SE = 0.64, $P = .373$) (Tables I and III). Additional adjustment for weight, physical activity, and dairy intake did not change the association.

Topical tacrolimus and pimecrolimus use

In all, 46.7% of the patients had used either topical tacrolimus or pimecrolimus in the previous 5 years. Median use was 120 g in the previous 5 years (Table II), and use was often restricted to several weeks or months. No child had used topical tacrolimus or pimecrolimus continuously.

Fractures

In all, 25% of the patients had a history of one or more bone fractures. No fragility fractures were reported. Lumbar spine Z-score was weakly correlated with the occurrence of fractures ($r = 0.27$, $P = .037$). Of the 3 children with a lumbar spine Z-score less than -2 only one child reported a bone fracture. Overall, patients in risk groups 1 to 4 did not have significantly more fractures (data not shown).

Biochemical parameters and BMD

Levels of serum calcium, albumin, phosphate, and PTH were normal in all patients.

A deficiency of 25-OH-vitamin D (<50 nmol/L) was found in 5 of 60 patients. In this group, all patients had a normal lumbar spine Z-score. Insufficiency of 25-OH-vitamin D (51-74 nmol/L) was found in 25 of 60 patients; 3 patients in this group had a low lumbar spine Z-score. Normal 25-OH-vitamin D (>75 nmol/L) was found in 30 patients, and in this group one patient had a low lumbar spine Z-score (Table IV). All patients received more than 10 minutes of sunlight daily. There was no

Table III. Association between lumbar spine Z-score and topical corticosteroid use/risk groups

	No. of patients per group	Univariate β (<i>P</i> value)	Multivariate β (<i>P</i> value)*
Cumulative topical corticosteroid use all classes in previous 5 y per kg	60	0.015 (.856)	0.105 (.260) [†]
Cumulative topical corticosteroid use all classes in previous 5 y per group of use	Low 33 Medium 14 High 13	Medium vs low 0.024 (.948) High vs low -0.124 (.746)	Medium vs low 0.200 (.582) [†] High vs low 0.248 (.567) [†]
Group 1 (risk + vs -)	-40 +20	0.220 (.486)	0.294 (.316)
Group 2 (risk + vs -)	-50 +10	-0.112 (.780)	-0.082 (.825)
Group 3 (risk + vs -)	-55 +5	-0.516 (.337)	-0.303 (.549)
Group 4 (risk + vs -)	-57 +3	-0.912 (.179)	-0.573 (.373)

*Adjusted for Z-score height.

[†]Adjusted for Z-score height, inhalation and oral corticosteroid use, cyclosporine use.**Table IV.** Laboratory parameters of *n* = 60 children with atopic dermatitis.

	Mean $\pm$ SD	Reference values*
Calcium, mmol/L	2.41 $\pm$ 0.06	2.17-2.64
Albumin, g/L	40.67 $\pm$ 2.52	34-50
Phosphate, mmol/L	1.45 $\pm$ 0.18	0.90-1.80
PTH, pmol/L	3.21 $\pm$ 1.04	1-7
25-OH-vitamin D, nmol/L	77.12 $\pm$ 27.08	>75

PTH, Parathyroid hormone; 25-OH-vitamin D, 25-hydroxyvitamin D.

*Age group-specific reference values are included in the reference values presented here.

statistical significant difference in lumbar spine Z-score and 25-OH-vitamin D levels (*P* = .858).

DISCUSSION

Children with moderate to severe AD may be at risk for having low BMD. We assessed several risk factors such as corticosteroid and cyclosporine use and lifestyle parameters for their potential to influence BMD in 60 children with moderate to severe AD. In this study we found that 4 of 60 (6.7%) children with AD had a low BMD (Z-score < -2) in the lumbar spine. The difference between the expected (2.5%) and observed (6.7%) percentage of children with a low BMD is not statistically significant. This means that we could not find evidence that low BMD occurs more frequently in this population of children with moderate to severe AD compared with the general population.

The amount of topical corticosteroids used in the previous 5 years by the patients in this study did not seem to be related to a decrease in BMD. This result is consistent with the outcome of the study done by

Pedreira et al⁸ in spite of methodological differences in calculating topical corticosteroids use. None of the 3 children with a low BMD had used more than 50 g of topical corticosteroids per month. The child with osteoporosis had even used less than 30 g of topical corticosteroids per month. Overall, the use of topical corticosteroids in our study population was low according to the practical guideline on topical corticosteroid use in children.²⁴ Furthermore, quantification of topical corticosteroids by pharmacy records can lead to an overestimation of the actual use, as these only represent the amount of topical corticosteroids prescribed by the dermatologist. Finally, the limited sample size of this study may have contributed to this finding and future studies should be performed in larger patient groups.

We did not find a negative association between additional use of inhalation/nasal corticosteroids and BMD (group 1). Data on the association between inhaled corticosteroids and low BMD are contradictory. Kelly et al²⁵ reported reduced bone mineral accretion in male children with asthma through puberty. Other studies found that long-term (2-6 years) inhaled corticosteroids had no significant effect on BMD.^{26,27} In the current study the number of patients using inhalation/nasal corticosteroids may be too small to detect any effect on BMD. Furthermore, the lifelong cumulative amount of inhalation/nasal corticosteroids was not available.

BMD tended to decrease when children had used systemic treatment in addition to topical/inhalation/nasal corticosteroids, especially when children were treated with both oral corticosteroids and cyclosporine in the previous 5 years (group 4). Pedreira et al⁸ also found a decreased BMD in children with moderate to severe AD, associated with the use of

cyclosporine ($n = 6$). Comparison with our data is difficult because children using inhalation or oral corticosteroids at inclusion were excluded and data on the use of these drugs in the past were not given in the study of Pedreira et al.⁸ Furthermore, the authors did not express BMD in Z-scores. A limitation in our study is that the number of children using additional systemic treatment is low.

A role for cyclosporine in inducing bone loss is identified in organ transplant recipients²⁸ and in patients with rheumatoid arthritis²⁹ but the exact mechanism involved in cyclosporine-induced bone loss is not well defined. Because the pharmacologic mechanism of topical tacrolimus and pimecrolimus is similar to that of cyclosporine, we also calculated the cumulative amount of these drugs. Use of topical tacrolimus and pimecrolimus was, however, limited and statistical analysis on the influence of these topical immunomodulators on BMD was not done. Our data suggest that the use of both oral corticosteroids and cyclosporine in combination with topical/inhalation corticosteroids may be associated with a trend toward a decrease in BMD. However, larger numbers of patients are needed to verify these results.

Haeck et al⁶ found a high prevalence (30.4%) of low BMD in adult patients with AD. No relation was found with cumulative topical corticosteroid use, even though the mean cumulative use was higher in the adult population than in the current child population (2687 vs 2044 g). Use of cyclosporine was not determined in the adult population. No difference in treatment duration was found between adults with a normal or low BMD. The definition of low BMD differs between adults and children, which hinders comparison. Haeck et al⁶ described low BMD in adults as a Z-score less than -1 in lumbar spine, or in one of the hips, whereas for children low BMD is described as a Z-score less than -2 in the lumbar spine. Furthermore, children have not yet reached their peak bone mass and catch-up bone mass acquisition can occur.³⁰ It has been suggested that juvenile bone mineral acquisition has little effect on adult bone density because the juvenile bone is largely replaced through growth.³⁰ Continued bone modeling and growth may make children less prone to low BMD. This may explain the difference in prevalence of low BMD between children and adults with AD. Serial BMD measurement, at least until peak bone mass is reached, in children with moderate to severe AD is necessary to investigate the difference in prevalence of low BMD with the results in adults.⁶

The influence of corticosteroids or cyclosporine on BMD was not confounded by other risk factors for

low BMD, such as dairy intake and physical activity. Low dairy intake, especially of cow's milk, is associated with low BMD.³¹⁻³³ In this population no association between the amount of dairy intake and BMD was found. However, we recorded the number of units of daily dairy intake, which is a rather crude technique. Use of the food frequency questionnaire and calculation of the daily calcium and vitamin D intake in milligrams is more accurate.³⁴ Physical activity can increase BMD, but it is not a major determinant of bone health.³⁵ In this population low physical activity was not associated with a decrease in BMD. In addition, biochemical parameters were assessed to exclude underlying bone disease. Levels of PTH, calcium, phosphate, and albumin were normal in all patients. Five patients had a 25-OH-vitamin D deficiency, but with normal PTH levels, and a normal BMD.

Adequate treatment of children with low BMD can prevent fractures later in life.³⁶ All 4 children with low BMD were supplemented with calcium/vitamin D. Therapeutic intervention with bisphosphonates should not be started on the basis of a single DXA measurement.³⁷ For this reason BMD measurement in the children with low BMD will be repeated.

This study shows that low BMD in children with moderate to severe AD does not occur more frequently compared with the general population. The cumulative amount of topical corticosteroids used in the previous 5 years was not related with a decrease in BMD in children with moderate to severe AD. Children with AD who were treated with oral corticosteroids and/or cyclosporine in addition to topical/inhalation/nasal corticosteroids in the previous 5 years tended to have a lower BMD, although this was not statistically significant.

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