

Does Breast Feeding Protect Against Later Overweight and Obesity?

Koletzko B., *Toschke A. M., **Vignerova J., **Osancova K., *von Kries R.

Department of Pediatric, Dr. von Haunersches Kinderspital,
Ludwig-Maximilians-University of Munich, Germany

*Institute for Social Pediatrics and Adolescent Medicine,
Ludwig-Maximilians-University of Munich, Germany

**National Institute of Public Health, Prague, Czech Republic

Obesity is now considered a global because its prevalence in both adults and children is increasing worldwide at an alarming rate (1 - 7). This increase is occurring not only in affluent countries but also in countries in economic transition and in developing countries. It has been related to an increasingly sedentary lifestyle with less physical activity, as well as to changing dietary habits (6, 8 - 11). Obesity has marked adverse effects in childhood and adolescence as well as long term effects that extend well into adulthood. Obese children often experience psychosocial distress and, in many cultures, considerable discrimination. Obese adolescents are at a clear disadvantage with respect to completion of advanced education, household income achieved in adulthood, and rates of marriage (12, 13). Obesity during childhood and adolescence affects the cardiovascular risk factors of dyslipidemia, glucose intolerance, and arterial hypertension.

Dyslipidemia, with increased concentrations of plasma triglycerides and low density lipoprotein cholesterol and reduced high density lipoprotein cholesterol, is a common finding in young obese individuals (14, 15). Obesity causes reduced insulin sensitivity, pathological glucose tolerance, and increased fasting and postprandial blood glucose concentrations, and it appears to play a key role in the marked increase of non-insulin-dependent diabetes mellitus recently observed in some pediatric populations (16).

Other consequences of early obesity are non-alcoholic steatohepatitis, which is not always benign but may result in cirrhosis (17, 18), cholelithiasis, pseudotumor cerebri, sleep apnea (which may be associated with neurocognitive deficits), disorders of the musculoskeletal system, and orthopedic complications with an increased long term risk of arthrosis, as well as polycystic ovary disease (15).

Persistence of childhood obesity into adult life is common. It has been estimated that between one third and two thirds of all obese children become obese adults, whereas about one third of adult obesity develops from obesity already manifest in childhood (19, 20). The risk of persistent obesity increases with increasing age of the child, the degree of obesity, and the presence of parental obesity (21). Persistence of obesity during adult life is associated with markedly increased morbidity and mortality (22, 23). It is of interest that childhood obesity is also reported to be related to an increased morbidity risk in adulthood even if obesity does not persist into adult life (24, 25).

In view of these marked adverse effects of childhood obesity, the fight against this new epidemic has become a prime objective for pediatric health care (1, 2, 26). As

available therapeutic interventions in obese children aiming at weight loss are costly and have less than satisfactory long term success rates, identification of strategies for effective prevention of obesity is particularly attractive.

Early Metabolic Imprinting

Although genetic predisposition is of major importance for an individual's risk of becoming obese (27, 28), the rapid increase in obesity prevalence in many parts of the world provides evidence for the strong modulating effects of exogenous factors. In addition to current lifestyle factors, events during early life appear to modulate later obesity risk, a phenomenon referred to as metabolic programming (29) or metabolic imprinting (30).

Indications for the existence of metabolic imprinting of obesity were provided by Ravelli and coworkers, who studied a cohort study of 19-year-old men at military induction who had been exposed during perinatal life to the Dutch famine of 1944-1945 (31). In this cohort, maternal exposure to famine during the last trimester of pregnancy and the first months of life was related to significantly lower obesity rates, while exposure during the first half of pregnancy resulted in a higher obesity prevalence than in non-exposed control (31). A later follow up study of women and men at age 50 years who were either exposed or not exposed to famine in late, mid, or early gestation reported a significantly higher body mass index (BMI) in exposed than non-exposed women, whereas there was no significant difference in men (32). Also, children of Pima women with diabetes during pregnancy were found to have a higher risk of later obesity than children of mothers who did not suffer from gestational diabetes, which persisted after correction for other influencing factors (33). The findings cited suggest that metabolic perturbations of regulatory systems established in early gestation contribute to the development of obesity in later life.

In view of these results, we have recently addressed the question of whether prolonged breast feeding might have long term programming effects on the prevalence of overweight and obesity in children at school entry (34). In this study - carried out in the state of Bavaria, Germany - the risk for overweight and obesity was decreased by exclusive breast feeding. Here we aim to summarize the results of that study, discuss whether the apparently reduced risk for overweight

and obesity in breast-fed children can be attributed to the properties of human milk, give further details on the lower prevalence of overweight/obesity in breast-fed children in Bavaria, and stimulate discussion as to which components of human milk might be instrumental in reducing the risk of obesity in breast-fed children.

Study Design and Setting

The study was performed as part of the Bavarian school entry health examinations 1997 enrolling 134,577 children (Fig. 1). From February 1997 to August 1997 some 13,345 children examined in two rural Bavarian regions (Oberpfalz and Niederbayern) and their parents were given a questionnaire on risk factors for atopic diseases. The overall response rate by the parents was 76.2%. The total number of completed questionnaires was 10,163. These data were linked to data on length and weight, measured as part of the routine health examination. The BMI was calculated as weight (kg)/height² (m). The analysis was confined to 5 year old ($n = 1975$) and 6 year old ($n = 7382$) German children, resulting in 9357 questionnaires for the analyses. The age and sex specific distribution of the BMI in all German children investigated during the 1997 school health examination in Bavaria was used as the reference to define overweight (BMI > 90th centile) and obesity (BMI > 97th centile).

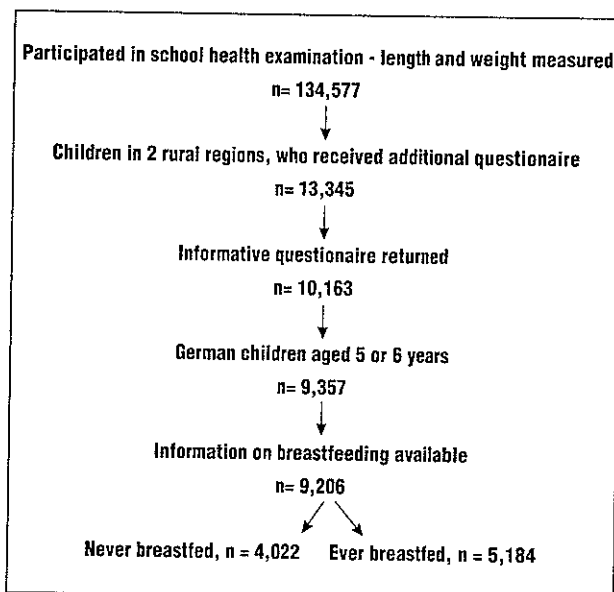


Fig. 1. Schematic depiction of the study population derived from the obligatory school health examination in Bavaria in 1997.

The main exposure was exclusive breast feeding and its duration. The question on breast feeding was: „Was your child breast-fed?“ If the answer was yes, the further question was: „For how long was your child exclusively breast-fed?“ The categories offered in answering this question were: for not more than 2 months; 3 to 5 months; 6 to 12 months; and for more than a year.

In order to identify covariables potentially associated with breast feeding, several additional items were considered. These included housing characteristics and lifestyle (for example,

the age of the house, whether the child had a separate bedroom, maternal smoking in pregnancy, spare time spent outside in summer and winter), questions on the child's health (prematurity, low birthweight), questions on diet (time of introduction of solid foods, consumption of own cooked food or industrial ready-to-feed products, food bought in health food shops), and quantitative questions (never, less than once weekly, once or twice, three to six times weekly, or daily) on the consumption of selected dietary items (milk products, fish, meat, fat, carbohydrates). The highest education of either parent was used as a marker of social class.

Main Results

The duration of breast feeding was associated with a progressive reduction in the prevalence of overweight – and even more so of obesity – in children at school entry (Fig. 2). Previously breast-fed and non-breast-fed children differed significantly in several indicators of social class and lifestyle. Many of these were also associated with overweight or obesity. High parental education, prematurity, and low birthweight were associated with a reduced risk of overweight and obesity, whereas maternal smoking during pregnancy was related to an increased risk. Full fat milk products (milk, quark or yoghurt, whipped cream) and sweet deserts may be avoided by overweight children, suggesting a spurious „protective“ effect of these products as compared to a „risk“ associated with the consumption of the low fat version of these products. There was also an apparent reduction of the risk of overweight and obesity associated with a high consumption of butter and breakfast cereals (34).

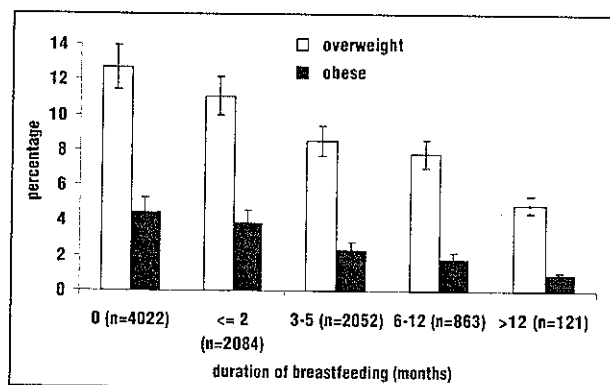


Fig. 2. Relation of breast-feeding after birth to overweight (BMI > 90th centile) and obesity (BMI > 97th centile). Prevalence in German children aged 5 or 6 years.

Parental education was the only factor accounting for a > 10% shift of the odds ratio for breast feeding and overweight and obesity towards unity. Other factors which remained significantly associated with overweight/obesity in the final logistic regression model were high parental education, maternal smoking during pregnancy, low birthweight, having a separate bedroom for the child, and frequent consumption of butter (Table 1). The adjusted odds ratios by duration of breast feeding are shown in Fig. 3. Being ever breast-fed reduced the risk of overweight by more than 20%, and breast feeding for 6 months or more reduced the risk by over 35%. Even more pronounced effects were observed with respect to obesity (25% and 43%, respectively).

Table 1. Factors associated with breast-feeding and overweight and obesity in 5 or 6 year old German children and their impact on overweight and obesity (only significant factors in a logistic regression model with breast-feeding included) *at least 10% change of the OR for breast-feeding and overweight/obesity.

	Prevalence in		Overweight		Obesity	
	not breast-fed children	breast-fed children	OR	90% CI	OR	90% CI
High parental education*	41.4%	66.7%	0.77	0.67 - 0.89	0.62	0.49 - 0.79
Maternal smoking in pregnancy	12.8%	4.2%	1.51	1.20 - 1.89	1.82	1.28 - 2.58
Prematurity	13.8%	9.0%	0.78	0.62 - 0.98	0.69	0.46 - 1.03
Birthweight < 2500 g	10.4%	6.6%	0.69	0.48 - 0.84	0.78	0.54 - 1.10
Own bedroom	45.6%	54.4%	1.19	1.03 - 1.37	1.22	0.96 - 1.56
Margarine >= 3 times per week	35.3%	32.4%	1.22	1.05 - 1.41	1.21	0.94 - 1.56
Butter >= 3 times per week	60.5%	69.2%	0.73	0.63 - 0.83	0.70	0.56 - 0.88
Full fat milk >= 3 times per week	50.8%	59.6%	0.69	0.60 - 0.80	0.54	0.42 - 0.68
Low fat milk >= 3 times per week	31.9%	28.8%	1.72	1.49 - 1.99	1.77	1.38 - 2.25
Full fat quark or yogurt >= 3 times per week	28.8%	36.1%	0.66	0.56 - 0.78	0.52	0.38 - 0.70
Low fat quark or yogurt >= 3 times per week	25.9%	23.8%	1.42	1.22 - 1.66	1.32	1.02 - 1.71
Whipped cream >= once per week	18.6%	24.7%	0.65	0.54 - 0.79	0.58	0.41 - 0.81
Breakfast cereals >= 3 times per week	25.6%	35.3%	0.80	0.68 - 0.93	0.76	0.58 - 0.99
Sweet deserts >= 3 times per week	54.4%	57.8%	0.84	0.74 - 0.97	0.82	0.66 - 1.03

Is the Reduced Risk for Overweight and Obesity in Breast-fed Children Related to Properties of Human Milk?

With all cross sectional studies there is a risk of recall/information bias. Some misclassification of the duration of breast feeding is likely when mothers have to remember details of their child's earlier feeding. This misclassification, however, is unlikely to be related to the outcome, because the overt aim of the study was the search for risk factors of atopic disease. Selection bias is also unlikely - the return rate of the questionnaires was high and unrelated to the outcome measure (34). Random misclassification of the measurement of height and weight is probable, as it is difficult to ensure that all persons involved in the measurement in more than 10 different public health offices used exactly the same equipment in exactly the same way. This misclassification, however, is unlikely to be dependent on breast feeding, as that information was not known to the persons involved in the measurement.

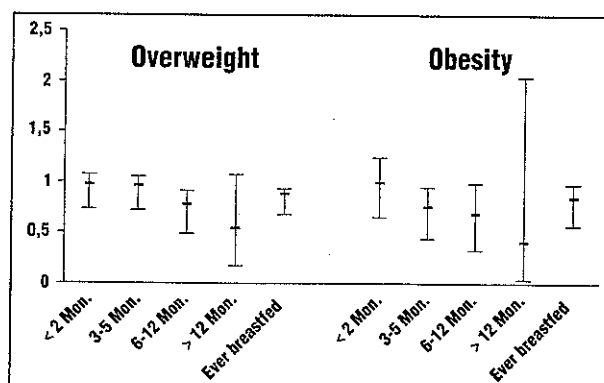


Fig. 3. Impact of the duration of breast feeding on odds ratio for overweight and obesity in German children aged 5 or 6 years. Odds ratios are adjusted for parental education, maternal smoking in pregnancy, low birth-weight, own bedroom, and frequent consumption of butter.

Breast feeding was associated with various lifestyle and dietary factors documented as part of the study. With the

Table 2. Prevalence (95% CI in brackets) of overweight (BMI > 90th percentile) and obesity (BMI > 97th percentile) in German children aged 5 or 6 years living in two rural Bavarian regions in relation to breast-feeding.

		Overweight %	Obesity %
Never breast-fed	(n = 4,022)	12.63 (12.36 - 12.90)	4.48 (4.38 - 4.58)
Ever breast-fed	(n = 5,184)	9.18 (9.02 - 9.34)	2.78 (2.73 - 2.83)
Breast-fed for:			
< 2 months	(n = 2,084)	11.13 (10.60 - 11.59)	3.79 (3.62 - 3.96)
3 - 5 months	(n = 2,052)	8.43 (8.06 - 8.80)	2.29 (2.18 - 2.40)
6 - 12 months	(n = 863)	6.84 (6.12 - 7.56)	1.74 (1.55 - 1.93)
> 12 months	(n = 121)	4.96 (1.14 - 8.78)	0.83 (0.16 - 1.50)

exception of parental education, none of these was a confounder of the association of breast feeding and overweight/obesity. High parental education in breast-fed children, however, only partially explained the association of breast feeding and overweight/obesity.

Information on important risk factors for overweight which might be confounders of the presumed protection by breast feeding could not be assessed optimally. These included lifestyle/social class and genetic risk factors for overweight or obesity.

Lifestyle and Social Class

Parental education may not be the optimal indicator of social class, but additional information is difficult to obtain in Germany because information on family income are not generally answered satisfactorily in Germany. Asking for family income may account for a selection bias by non-response although a potential impact of social class on health is not perceived by the German population.

Physical activity is certainly an important risk factor for overweight/obesity. As the questionnaire had not been originally designed for this purpose these questions were limited to „time for playing outdoors“, which - though associated with breast feeding - was not associated with overweight/obesity and was not a confounding variable.

Diet is another important lifestyle factor associated with the risk of adiposity. The questions on this were confined to a semi-quantitative assessment of the present diet. Many overweight children, however, might have changed diet to reduce their weight.

Genetic Risk Factors for Overweight/Obesity

Parents' weight is an important indicator of the genetic risk for overweight/obesity (27, 28), and maternal overweight appears to be associated with a short duration of breast feeding or no breast feeding (35). A positive family history of adiposity was not a confounder of the association between breast feeding and overweight/obesity in a previous study (36). After the publication of our results, the issue was investigated in another prospective cohort study, the German multicenter allergy study (MAS) (37, 38). In the MAS cohort, longer breast feeding was less common in overweight mothers, but maternal overweight was not a confounder of the association of breast feeding and overweight/obesity.

A strong argument against lifestyle factors explaining the observed protective effect of breast feeding comes from a stu-

dy by Kramer on Canadian adolescents born in the 1960s (36). In that study a similar dose-related, protective effect of breast feeding on the later prevalence of overweight/obesity was found. If such a dose-dependent protective effect were caused by lifestyle factors associated with breast feeding, similar confounding factors should have to have been operative during the different time periods in different societies. In Kramer's study only 18.5% of the children had been breast-fed, compared with 56% our study, suggesting that the mothers who chose to breast feed their children in the 90s in Bavaria formed a different population from those who chose to breast feed in the 60s in Canada. The lifestyle in the early 60s in Canada was almost certainly different from that in Bavaria in the early 90s. Although it is difficult to rule out the possibility that unknown factors associated with the lifestyle of families of breast-fed children might play a causative role in the apparent protective effect of breast feeding, this does not appear likely.

Body Mass Index of the Children Studied

The age and sex specific distribution of the BMI in all German children investigated during the 1997 school health examination in Bavaria was used as the reference to define overweight (BMI > 90th centile) and obesity (BMI > 97th centile). The 90th and 97th centiles in Bavaria are considerably higher than the widely used French reference values (39) (Table 2). Thus most children defined as overweight according to the Bavarian centiles would have BMI values above the 95th centile of the French reference values.

The lower prevalence of overweight/obesity in breast-fed children in Bavaria does not reflect a shift in the entire distribution of the BMI in breast-fed children as compared with formula-fed children. There is no shift of the mean but the upper tail of the distribution is „fatter“ in non-breast-fed children (Fig. 4). This has implications for other studies in that our findings might not be reproduced if only means and their 95% confidence intervals are considered. The biological model to explain the observed protective effect on overweight and obesity should match a shift in the „upper tail“.

As our study was cross sectional, we do not have data on the longitudinal evolution of BMI during the first 5 years of life in these children. However, such longitudinal data are available from the analysis of the prospective German MAS

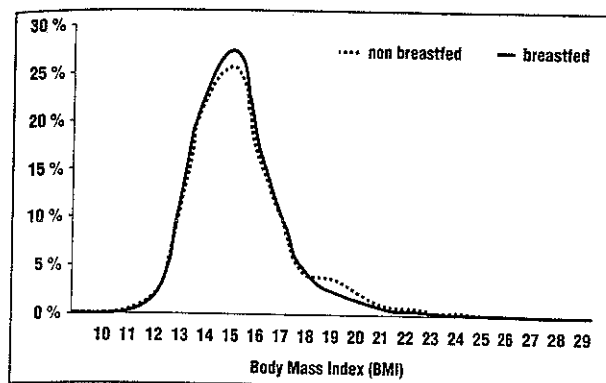


Fig. 4. BMI distribution in breast-fed and non-breast-fed German children aged 5 and 6 years.

study (37, 38). It is of interest that the BMI data from the MAS cohort show that differences between the subgroups which had been breast-fed for less than 2 months or for at least 2 months, respectively, only evolved after the fourth year of life - that is, at the time of BMI rebound (38). Thus other studies that observe children aged less than 5 years might not be able to detect any BMI differences related to postnatal feeding.

Is a Protective Effect of Breast Feeding also Detectable in Populations under Different Living Conditions?

In cooperation with Drs. Jana Vignerova and Katerina Osancova, National Institute of Public Health, Prague, Czech Republic, and Dr. Lida Lhotska, IBFAN/Geneva Infant Feeding Association, Geneva, Switzerland, we had the opportunity to evaluate data from a cohort of Czech children studied with support by the Internal Agency of the Ministry of Health, Czech Republic (registration number 0268-3) (40). Cross-sectional survey data were collected in 1991 on 33,768 school-children aged 6 to 14 years in the Czech Republic. The data were analyzed using multiple logistic regression analyses. The main outcomes chosen were overweight defined as BMI > 90th percentile and obesity defined as BMI > 97th percentile. The results of the analysis show that children who had ever been breastfed had a lower overall prevalence of overweight (9.3%; 95% CI 8.9 - 9.6%) than children that were never breastfed (12.4%; 95% CI 11.3 - 13.6%). Similarly, the prevalence of obesity was clearly lower in previously breastfed children (3.2%; 95% CI 3.0 - 3.4%) compared to previously formula fed children (4.4%; 95% CI 3.7 - 5.2%).

The effect of breastfeeding on overweight/obesity did not diminish with age in children 6 to 14 years old and could not be explained by parental education, parental obesity, maternal smoking, high birthweight, watching TV, number of siblings and physical activity. Adjusted odds ratios for breastfeeding were 0.80 (95% CI 0.71 - 0.90) for overweight and 0.80 (95% CI 0.66 - 0.96) for obesity. Thus a reduced prevalence of overweight/obesity was also detectable in an Eastern European country at a time with living conditions influenced by a socialist society. This suggests that the protection conferred by breastfeeding is not related to factors associated with breastfeeding in Western European capitalist societies and

makes it more likely that compositional aspects of human milk may play a causal role.

Are There Components in Human Milk that Reduce the Risk of Obesity in Breast-fed Children?

Features of human milk feeding that might account for a lower risk for overweight/obesity in breast-fed infants could include hormonal responses, bioactive factors in the milk, a lower energy intake, or a lower protein intake, all of which might have long term effects.

Lucas et al. (41, 42) reported significantly higher plasma insulin concentrations in formula-fed than in breast-fed infants, which would be expected to stimulate fat deposition and thus affect the early development of adipocytes. Human milk also contains bioactive factors that may modulate tissue growth and development. Breast milk contains both epidermal growth factor and tumor necrosis factor α , both of which are known to inhibit adipocyte differentiation *in vitro* (34).

Nutrient intakes of breast-fed and formula-fed infants differ. Recent data indicate that the metabolizable energy and protein intakes of breast-fed infants are considerably lower than previously assumed and significantly below those found in populations of formula-fed infants (34). These early differences in macronutrient supply might have long term effects on substrate metabolism. In longitudinal follow up studies, Rolland-Cachera and coworkers observed a significant relation between the dietary protein intake at the age of 10 months with later BMI and body fat distribution (43, 44). These investigators proposed that a high protein intake in early childhood might predispose to an increased risk of obesity at a later age. Indeed, in animal studies the early protein availability during fetal and postnatal development was found have long term metabolic programming effects on glucose metabolism and body composition in adult life. Whether or not postnatal intake of protein or other substrates does indeed affect later body composition needs to be tested in properly designed prospective trials.

European Commission Research Project on „Childhood Obesity - Programming by Infant Nutrition (CHOPIN)“

The EU Childhood Obesity Programme is a prospective multicenter trial with the aim to investigate whether the protein content and protein/fat ratio in infant formula and complementary feeds has lasting effects on later obesity risk. A one year multicentre intervention trial starting in the neonatal period will be performed in five European countries (Belgium, Germany, Italy, Poland, and Spain) with different habitual total protein intakes from complementary feeds to increase the range of protein intakes and thus to improve the statistical power to test the „early protein hypothesis“ (www.danoneinstitute.org/Euchildhoodobesity). With a total budget of 2.8 million EUR, the EU Childhood Obesity Programme will study, over the first two years of life, body compo-

sition, hormonal status, protein metabolism, and new, simple anthropometric markers of childhood obesity. In addition, the whole study cohort will be followed up until the ages of 8 years. If a relationship between early feeding characteristics and later childhood obesity risk will be confirmed, it will offer the possibility for obesity prevention, for improving dietary advice to parents, and for developing nutritionally improved dietary products for infants.

Conclusions

Based on the data from this cross sectional study enrolling almost 10,000 children, there is strong evidence that breast-fed children are less likely to be overweight or obese at school entry than formula-fed children. This effect reflects „fattening“ of the upper tail of the BMI distribution for non-breast-fed children but is not caused by a shift of the mean BMI. There are some indications that the reduced risk of overweight/obesity in breast-fed children might be related to properties of human milk and not to different genetic or lifestyle factors in these children. However, at present we cannot exclude the possibility that confounding variables such as parental BMI or other factors associated with breast feeding might play a role. The ongoing prospective EU Childhood Obesity Programme will offer an opportunity to test whether macronutrient composition of early feeding has a role to play in modulating long-term obesity risk.

Acknowledgements

The work of the authors is financially supported in part by the Bavarian Ministry of Health, Munich, Germany; the Child Health Foundation, Munich, Germany; the European Commission, General Directorate Research (QLK1-2001-00389); and the Ministry of Health, Czech Republic (registration number 0268-3).

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*Berthold Koletzko, MD, Professor of Pediatrics
Kinderklinik and Kinderpoliklinik, Dr. von Haunersches
Kinderspital
Ludwigs-Maximilians-University of Munich
Lindwurmstr. 4
D-80337 München
Germany
e-mail: cwellbro@helios.med.uni-muenchen.de*

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Čes.-slov. Pediatr., 58, 2003, No. 1, p. 9.

Fedor M., Minarik M., Kunovský P. a kol.: Intenzivná starostlivosť v pediatrii. Martin, Vydavateľstvo Osveta 2002. 434 s.

Ide o druhé doplnené vydanie príručky pre lekárov zaoberajúcich sa najmä intenzívnou starostlivosťou v pediatrii. Knižka však slúži tiež ako zdroj kumulovaných informácií pre lekársku obec vo všeobecnosti ako tiež pre študentov medicíny. Náklad prvého vydania z r. 1999 bol menší ako dopyt a rýchlo sa rozobral. Veľmi potrebná príručka vznikla na základe dlhoročných skúseností autorov, pracujúcich na JIS KDaD v Martine (Fedor, Minarik), v Kardiocentre Bratislava (Kunovský) a ďalších pracoviskách v ostatných centrách, vrátane neonatológie, detskej chirurgie, ARO, transportnej služby a i.

Kniha obsahuje nasledovné kapitoly: Kardiopulmonálna resuscitácia, diagnostika a liečebné výkony, naliehavé stavy a syndrómy, úrazy, otravy, pneumológia, kardiológia, nefro-

lógia (včítane eliminačnej liečby), neurológia, endokrinológia, gastroenterológia, metabolizmus a výživa, dávkovanie liečiv a fyziologické hodnoty a nomogramy. Jednotlivé kapitoly sú spracované z pohľadu charakteristiky kritických stavov, ich etiopatogenézy a liečby, resp. zo súhrnu informácií referenčných hodnôt a odporúčaných dávok liečiv. Kniha obsahuje zoznam telefónnych čísel (kontaktov) na pracoviská intenzívnej medicíny v SR, prevozovej služby, zoznam použitých skratiek a i. Chýba však register, ktorý pre veľké množstvo údajov by bol veľmi rozsiahly, čo by predražilo vydanie.

Ide o veľmi vydarené, potrebné a informujúce dielo. Knižka je vreckového formátu, má mäkkú väzbu (obal), čo umožňuje mať ju pri sebe. Dielo odporúčam do pozornosti pediatickej obci. Gratulujem hlavnému zostavovateľovi, zostavovateľom a autorom (celkom 10) k vydarenému počinu, ako tiež vydavateľovi za výbornú grafickú úpravu.

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