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Low Birth Weight and Preterm Birth: The Emerging Importance of Prevention

Earl Siegel¹, University of North Carolina at Chapel Hill, USA

Traditionally the infant mortality rate has been accepted as an index of a society's general level of development, including its commitment to improved child health and development. Recently the significance of low birth weight (LBW) as a community health indicator and more specifically as a determinant of neonatal mortality and childhood morbidity has become widely appreciated [1]. Childhood morbidity is especially noteworthy in the developed countries where applications of advances in perinatal medicine have been associated with sharp increases in LBW survivors.

LBW, defined as less than 2500 g, is highly correlated with preterm births that occur at less than 37 weeks gestation. Full-term intrauterine growth retardation (IUGR) accounts for as much as one-third of LBW infants in developed countries, increasing to one-half among their low socioeconomic status populations [2]. Very low birth weight (VLBW) infants, who weigh less than 1500 g and are consistently preterm, explain most of variation in neonatal mortality and childhood morbidity [3–8]. Therefore, VLBW infants represent the group of greatest concern among the categories of LBW.

The causes of the several types of LBW are poorly understood, complex, and interrelated. The purpose of this article is to document the importance of the problem, present an attractive conceptual model regarding major risk factors associated with it, and identify promising prevention strategies. For the most part, data and experiences drawn from the English

language literature will be cited. But, to some degree at least, the interventions should also pertain to other industrialized countries. Attention will be directed to the interests of social and preventive medicine specialists, medical practitioners and public health nurses as well as maternal and child health specialists.

Importance of Low Birth Weight

Neonatal Mortality

In 1980 6.8% of all live-born infants in the United States weighed less than 2500 g and 1.2% less than 1500 g [9]. The incidence of LBW among nonwhites was twice that of whites—12.5 vs 5.9%; VLBW also was much higher in nonwhites—2.4 vs 0.9% [9]. *Table 1* shows LBW and VLBW ratios for 12 other developed countries, indicating the relative seriousness of the problem in the United States, but the urgent need for its prevention everywhere will be amply documented. Studies have repeatedly shown that low birth weight infants account for two-thirds of neonatal mortality. LBW infants are almost 40 times more likely to die in the neonatal period than normal birth weight infants, while the relative risk for VLBW infants is 200 times greater [3–6]. As already noted, in the last decade LBW and VLBW-specific mortality rates have decreased dramatically. Birth-weight-adjusted mortality rates, comparing United States and Swedish trends, illuminate the differing dimensions of the problem. In Massachusetts [10] and North Carolina [11] neonatal mortality rates appear to be considerably higher than Sweden, with LBW proportions almost twice as high. However, when the two states' mortality rates were adjusted to the Swedish birth weight distributions, Massachusetts' and North Carolina's mortality rates became lower than Sweden's. Detailed analyses of

¹ Professor of Maternal and Child Health
Clinical Professor of Pediatrics
School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27514, USA.

Table 1. Percent of VLBW and LBW live births in selected developed countries, 1980

Country	VLBW	LBW
Austria	0.80	5.68
Canada ¹	0.84	6.10
Denmark	0.72	6.00
Federal Republic of Germany	0.71	5.51
German Democratic Republic	0.55 ²	6.19
Israel	0.99	7.16
Italy	0.83	6.71
Japan	0.39	5.18
New Zealand	0.65	5.27
Norway	0.59	3.25
Sweden ³	0.49	4.03
Switzerland	0.56	5.14
United Kingdom		
England and Wales	0.77	6.79
Scotland ⁴	0.96	6.73
United States	1.15	6.84

¹ Data for 1979; ² Probably an underestimate attributed to a non-standard definition of live births and late fetal deaths; ³ Data for 1978; ⁴ Data from 1977 to 1981.

Adapted from: Institute of Medicine, Preventing Low Birth Weight, National Academy Press, 1985.

neonatal mortality and birth weight distribution trends also have been carried out for the United States as a whole [3], for California [4], and for North Carolina [5]. The studies used different analytic strategies, but the findings were similar. Declines in neonatal mortality, particularly over the last decade, were the result of reductions in low-birth-weight-specific mortality, with minimal improvements in birth-weight or gestational-age distributions. Thus, the neonatal mortality declines appear largely attributable to neonatal intensive care of VLBW infants—tertiary level interventions that carry large economic costs, with substantial burdens for survivors and their families. The case for prevention in relation to neonatal mortality is clear.

Survivors of the Neonatal Period

What are the experiences of LBW survivors of the neonatal period? They are five times more likely to die during the postneonatal period than normal birth-weight-infants [7, 12]. VLBW infants are at 20 times greater risk of dying [7, 12]. Moreover, about 20% of present day postneonatal mortality is directly related to “delayed” neonatal deaths, representing the rapidly increasing proportions of VLBW infants who are delivered at, or transferred to regional perinatal intensive care centers [13, 14].

Perhaps the most important consequence of LBW is the increased risk of long-term morbidity. The major concern has been neurologic and developmental handicap, which is three times more likely in LBW than normal birth weight infants [15]. Follow-up studies since the introduction of neonatal intensive care suggest that improved survival of VLBW infants is not associated with increased relative risk of long-term neurologic or developmental morbidity [16, 17]. But nonetheless, 10% of VLBW infants are severely

affected and an additional 25–30% are moderately or mildly handicapped [8, 18–20]. Significantly, the considerable decline in VLBW mortality rates probably will yield larger numbers of handicapped preschool and school-aged children who will require specialized medical, rehabilitative, and educational services. Furthermore, it is clear that the antenatal environmental factors which increase the incidence of LBW and VLBW among low-socioeconomic-status mothers also operate postnatally and contribute to poor cognitive and social development among survivors [21–23].

Major congenital anomalies are the second most common morbidity among LBW infants, who are at three times greater risk than normal birth weight survivors, with IUGR infants at the greatest risk [24–26]. (It might be that LBW is a consequence of the anomaly.) Chronic pulmonary disease [27, 28] and retrolental fibroplasia [29, 30] are severe, though less frequent morbidities associated with VLBW survival.

The medical conditions noted and others that plague the health and development of VLBW infants result in rehospitalizations for about one-third of them, compared to 17% of normal birth weight infants [7, 31, 32]. The psychosocial [22, 33–36] and financial stresses [37] that families of VLBW infants experience also are substantial.

Costs of Care

Clearly, health status burdens imposed on the young children and families of low-birth-weight and preterm infants are extremely high. Economic costs of caring for VLBW infants have been investigated, using several methodologies. In an article with the apt title, “Womb Rent”, average costs were ascertained for newborn care based on completed weeks of gestation [38]. In 1973–77 it cost over \$60,000.— for care of a premature infant of 25 to 26 weeks gestation, dollar costs declining as gestation increased. At 32 to 33 weeks gestation, the cost was \$20,000.— per infant. The dramatic reductions in costs associated with increasing gestational age and birth weight are compellingly apparent. That the cited expenditures are for the early 1970s warrants emphasis, given escalating costs derived from inflation and new technologies introduced since that time.

A different economic perspective is gained from a population-based, cost-benefit analysis of regional neonatal intensive care [39]. Using historical controls, the authors projected total cost, not only that of initial hospitalizations. Included are later medical, rehabilitative and special education costs of VLBW infants, which were compared with expected earnings and productivity. Based on these cost computations, it was concluded that there was a net economic benefit for infants over 1250 g. However, below that birth weight the cost of care of nonsurvivors and acute and long-term care of chronically handicapped survivors was not justified in economic terms. The gap was greatest for 750 to 999 g infants who survived the longest in the nursery. Those weighing less than 750 g had fewer

survivors and the survivors died sooner. Thus, costs were lower for latter group. These painstakingly accumulated detailed cost findings, confirmed by others [40, 41], create serious ethical conflicts as society seek to allocate its health care resources.

The urgent need for preventive strategies cannot be ignored, given the mortality, childhood morbidity, and fiscal consequences of preterm birth, LBW and VLBW.

A Sociobehavioral Model

Bragonier, Cushner, and Hobel recently hypothesized a group of maternal risk factors that trigger preterm labor [42]. Also represented are factors associated with IUGR as well as preterm birth. Figure 1 shows frequently documented sociobehavioral and medical maternal risk factors, with stress and inadequate social supports occupying a central locus in the model. The conceptual model is attractive because it integrates the interrelationships of the various maternal characteristics that lead to a progression of biologically determined events. These events, depicted as stages, suggest preconceptional, prenatal and early labor intervention strategies presented below. The authors' hypothesis has been described in detail elsewhere [43]. A useful summary [42] indicates the following: "Stages I and II are considered the silent stages of preterm labor. The conditions listed in Stage I and the biochemical changes occurring in Stage II lead to a more symptomatic stage IIIA, where uterine contractions cause prostaglandin synthesis in the decidual cells

and initiate a cascade of change [44]. Cervical effacement and dilatation then allow infection, if present, to ascend into the uterine cavity. Infection is a further stimulus to prostaglandin synthesis and the progression of changes that we describe as preterm labor.

The duration of the early stages of preterm labor (I and II) is variable and depends on the occurrence of risk factors and the ability of the patient to cope with or alter their effect. Stage III is thought to have a more defined duration, and since it is a symptomatic phase, patients at risk can be identified. Patients are thought to be in this symptomatic phase as briefly as 6–12 hours or as long as 1–2 weeks. It is not uncommon for patients admitted in preterm labor (Stage IV) to relate a history of Stage III symptoms for 1–2 days prior to calling their physician or health care provider. We believe this clinically oriented hypothesis of preterm labor is realistic and provides a basis for designing a program to prevent preterm delivery."

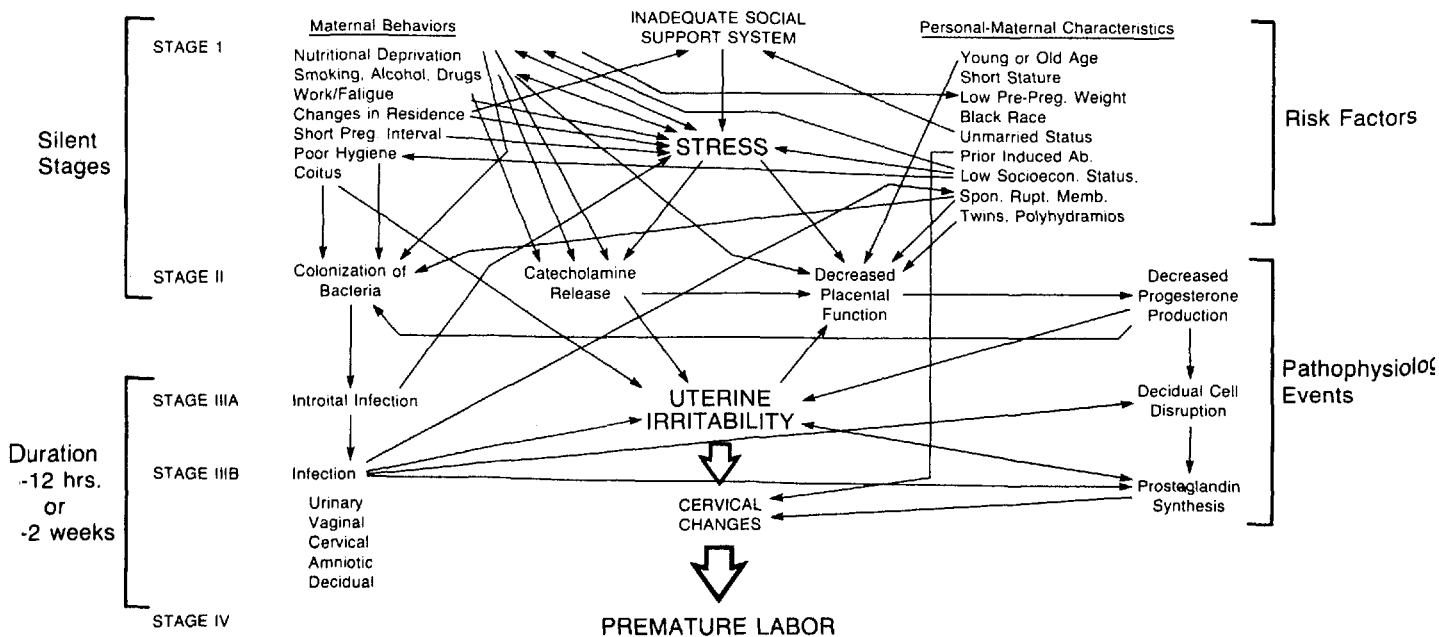
Specific documentation of the maternal-risk factors and their relationship to preterm labor as well as LBW will not be presented here. They are generously referenced by the authors [42] and by other reviewers [45–47]. Rather, the remainder of this article will focus on three preventive strategies that appear particularly promising.

Preventive Strategies

Given the central role of stress, inadequate social supports and low-socioeconomic-status risk factors, it

Figure 1

HYPOTHESIZED FACTORS INFLUENCING PRETERM BIRTH



ADAPTED FROM: BRAGONIER, R.J. CUSHNER, I AND HOBEL, C. SOCIAL AND PERSONAL FACTORS IN THE ETIOLOGY OF PRETERM BIRTH. IN PRETERM BIRTH: CAUSES, PREVENTION AND MANAGEMENT. FUCHS, F AND STUBBLEFIELD, P EDITORS. 1984.

is self-evident that social interventions are of highest priority in the reduction of preterm birth and low birth weight. Better education, income, jobs, social services, and community development would have a major impact on a number of Stage I factors. Despite the primacy of the societal changes required to affect them favorably, it appears appropriate in this article to focus on three promising preventive health care strategies.

Components of each strategy are presented. When evidence is available, effectiveness of the specific strategy will be cited.

Preconceptual Identification of those at Risk of LBW and Effective Methodologies for Reducing their Risk

Although the concept of high risk assessment as a part of prenatal care has been generally accepted for many years, preconceptual risk assessment to reduce preterm labor and low birth weight has been proposed only recently. Stage I risks such as poor nutrition, chronic illness, smoking, alcohol and drug hazards; being too young or too old (<17 or >35), short pregnancy interval; excess stresses; and inadequate social support systems can be recognized within the context of primary health care, before the onset of pregnancy. Specific interventions to reduce the risk can be undertaken as appropriate, including management of chronic illness, particularly undernutrition, hypertension, and diabetes; decreasing smoking and alcohol intake; stress reduction, and promoting effective family planning methods. Each intervention can play a role in risk reduction. Several reports of preconceptual interventions suggest their value [48, 49]. It is well known that women with previous LBW and preterm births are at considerably higher risk of repeating the experience [50]. Therefore, special efforts should attach to identifying these women and reducing their risk factors. In addition to primary health care providers in conventional settings, university and secondary school health services should incorporate preconceptual strategies in their practice protocols. Finally, family life and sex education programs should include approaches that emphasize reducing the risk behaviors suggested in Stage I of the model.

Assuring all Low-Socioeconomic Status Women of Early and Frequent High Quality Prenatal Care Visits

It seems reasonable to assume that routine prenatal care would have a favorable effect on the incidence of preterm birth and low birth weight. Documenting the relationship has been fraught with considerable methodological frustrations:

1. Experimental designs, controlling for the quantity and quality of prenatal care, have been perceived as unethical.
2. Most recent studies of the value of prenatal care have been based on statistical analyses that use the month or trimester care began and/or number of visits. But, because they deliver earlier, women having preterm births obviously will have fewer visits than

those having term births. Furthermore, the recommended prenatal care schedule includes more frequent visits at the end of the pregnancy. For these reasons, it is now conventional to adjust for gestational age [51]. The Kessner Index (Table 2) is based on the prenatal care recommendations of the American College of Obstetricians and Gynecologists. Adequacy of prenatal care use is assessed by the trimester care began and number of visits, adjusted for gestational age.

Table 2. Criteria for adequacy of prenatal care index (Kessner Index)

Adequacy of care	Gestation ^d (weeks)	No. of prenatal visits
Adequate ^a	13 or less	1 or more or not stated
	14–17	2 or more
	18–21	3 or more
	22–25	4 or more
	26–29	5 or more
	30–31	6 or more
	32–33	7 or more
	34–35	8 or more
	36 or more	9 or more
	Inadequate ^b	14–21 ^c
22–29		1 or less or not stated
30–31		2 or less or not stated
32–33		3 or less or not stated
34 or more		4 or less or not stated
Intermediate	All combinations other than specified above	

^a In addition to the specific number of visits indicated for adequate care, the interval to the first prenatal visit has to be 13 weeks or less (first trimester).

^b In addition to the specific number of visits indicated for inadequate care, all women who started their prenatal care during the third trimester (28 weeks or later) are considered inadequate.

^c For this gestation group, care is considered inadequate if the time of the first visit is not stated.

^d When month and year are specified but day is missing, impute 15 for day. Adequacy categories are in accord with recommendations of American College of Obstetrics and Gynecology and the World Health Organization.

Source: Kessner, DM: Infant death: An Analysis by maternal risk and health care, 1973, Washington, D.C.: National Academy of Sciences.

3. Selection bias must be considered since the same variables that motivate women to seek prenatal care also may influence the incidence of pregnancy outcome. Therefore, control for confounding variables is essential.

4. Few studies have collected data that measure the content or quality of care.

Using the Kessner Index and controlling for confounding variables, five separate studies have shown significant differences in birth weight or the incidence of LBW, favoring adequate prenatal care use [51–55]. Four of the investigations employed multivariate analyses, including major maternal risk factors in their models [52–55]. The most recent report confirms and extends earlier findings [55]. The authors found, using multiple regression data analytic techniques, that adequate prenatal care use was associated with an overall increase of 197 g in average birth weight. When only

babies of short gestational age (≤ 280 days) were included in the analysis, the association of adequate prenatal care with birth weight drops by 113 g. These intriguing findings suggest that adequate prenatal care use increases gestational age and consequently birth weight.

With regard to the quality of prenatal care, two research reports are pertinent, both employing quasi-experimental evaluation designs [56, 57].

Beginning in the mid-1960s, Maternity and Infant Care projects provided high-quality comprehensive prenatal care. These projects, limited to low income populations, incorporated not only obstetric care but also nutrition, social work, health education, public health nursing and community outreach services. In the Cleveland, Ohio, Maternity and Infant Care Project patients who received comprehensive care had significantly better outcomes than a group which was closely matched by risk factors but received only routine care without the support health services noted earlier [56]. The incidence of preterm birth among the comprehensive and routine care groups were as follows: 21–31 weeks—1.9 vs 3.0%, and 32–37 weeks—16.0 vs 19.7%, respectively. VLBW and LBW differences between the two groups also were highly significant, favoring comprehensive prenatal care.

In 1977 the OB Access Pilot Project was developed in Northern California to provide better access to comprehensive prenatal care for low socioeconomic status women who previously had minimal prenatal care [57]. Matching for socioeconomic and reproductive risk factors, the OB Access patients had better outcomes than the comparison group—VLBW, 1.3% vs 2.4% and LBW, 4.7 vs 7.1%, respectively. The OB Access evaluation findings were subjected to a detailed cost benefit analysis. Considering only neonatal intensive care and rehospitalization costs during the infant's first year of life, savings of \$1.70 for every dollar expended for comprehensive care were realized [58]. Longterm savings were not computed.

Early Identification and Prompt Treatment of Preterm Labor

This secondary prevention strategy consists of early prenatal identification and education of women at high risk of preterm labor. The rationale for the strategy derives from Stages III–IV of the sociobehavioral model described earlier. Successful intervention is dependent terminating, through the very early administration of tocolytic treatment, "the cascade of changes" that rapidly produce uterine irritability. Tocolytic agents have been shown to stop uterine contractions when given intravenously [59], but oral application has been relatively ineffective [60].

Current interest in the prevention of preterm birth focuses on initiation of treatment during Stages II and III before labor actually has begun. Therefore assessment of women at high risk becomes an obvious requirement. Papiernik, a French obstetrician, pioneered the development and refinement of such

procedures [61, 62]. Others, using risk factor data from their own populations, have employed modifications [63, 64] of his model.

The assessment instruments permit identification of high-risk women and interventions to reduce risk behaviors. High-risk patients and health providers also are thoroughly educated regarding the signs and symptoms of early preterm labor. Weekly visits, beginning at the 20th to 28th week of pregnancy, permit frequent cervical examinations, providing baseline findings to detect early signs of preterm labor. When the women and their obstetrical attendants suspect preterm labor, careful monitoring of contractions and the cervical status is carried out to determine whether significant changes have occurred. It appears that the cervical changes are related to preterm labor and subsequent preterm birth. With the onset of the changes, tocolytic treatment is initiated. Papiernik first developed such an intervention strategy in 1973 [65]. Over the subsequent seven years, a reduction in preterm births from 10.1 to 3.4% was experienced. It should be noted that in addition to the early identification of preterm labor and tocolysis, provision of social supports, rest and nutrition supplementation was a part of the intervention protocol. Also distant travel and changes in residence were discouraged.

A similar program was undertaken by Papiernik in Martinique, where the care was provided by nurse midwives, and over a three-year period preterm birth ratios declined from 6.0 to 4.4% [65].

In San Francisco, California, another program, paralleling Papiernik's, showed a reduction of the preterm birth ratio from 6.7 to 2.4% after three years [66]. No change was observed in a comparison, affiliated hospital where the program was not introduced.

In sum, this secondary preventive strategy, though promising, requires validation of its efficacy before it can be recommended for general dissemination. There are recognized costs to be assessed, including the weekly prenatal visits, hospitalizations for intravenous treatment, and occasional serious complications from use of the tocolytic agents. Despite the lack of well-designed evaluations, the Papiernik approach has been adopted by a number of states in the United States. Significantly, a randomized clinical trial among high-risk women has been designed and implemented as a collaborative, five-center research project, with the results expected by mid-1986 [67].

Summary

This article on LBW and preterm birth was prepared for this issue, "Interdisciplinary Strategies for Prevention", recognizing its US focus in relation to a European audience. Although the pregnancy and infant health magnitude of the problem is greater in North America, its multifactorial nature and serious impacts are experienced worldwide. Emphasis has been placed on its high costs vis-à-vis neonatal mortality, childhood morbidity, and medical care expenditures for tertiary level management.

Three preventive health care strategies, linked to an attractive sociobehavioral model, are presented. The model displays multiple risk factors and their interrelationships, including the pathophysiological events that lead to LBW and preterm birth. Acknowledging

the primacy of basic societal level changes, the strategies nonetheless are based in the health care services. They call for interdisciplinary interventions as a part of preconceptional and prenatal health care. Such approaches as reduction of stress and other risk behaviors, improved nutrition, family planning and social services as well as strengthening family and community support systems are suggested. In addition a secondary prevention strategy dependent on identification of pregnant women at high risk of LBW and preterm birth is described. Early recognition by patients and providers of signs of uterine irritability may enable prevention of preterm birth by prompt treatment with tocolytic agents. Evidence relevant to the effectiveness of the preconceptional and prenatal care interventions, insofar as it is available, is cited.

Résumé

Poids de naissance insuffisant et naissance avant terme: l'importance croissante de la prévention

Cet article, rédigé par un professeur de pédiatrie et de santé publique américain, s'il traite surtout de la situation aux Etats-Unis, est tout à fait pertinent néanmoins pour l'Europe occidentale. Bien que les risques qui menacent la santé de la mère (pendant la grossesse) et du nouveau-né soient souvent plus sévères en Amérique du Nord, leur nature multifactorielle et la gravité de leurs conséquences sont évidentes partout. Le coût élevé de la pathologie correspondante, en termes de mortalité néonatale, de morbidité infantile, et de dépenses médicales (surtout soins tertiaires – traitements dans des centres de référence) est souligné.

L'auteur présente trois stratégies préventives, liées à un stimulant modèle socio-comportemental. Ce modèle illustre les multiples facteurs de risque concernés et leurs relations, y compris les événements pathophysiologiques, qui mènent à un poids de naissance bas et à une naissance avant terme. Bien qu'elles reconnaissent la primauté de changements fondamentaux dans la société, ces stratégies sont basées sur les services de santé. Elles demandent des interventions interdisciplinaires aussi bien avant la conception de l'enfant que durant la période prénatale. Des approches telles que la réduction du stress et d'autres comportements à risque, l'amélioration de la nutrition et celle des services de planification familiale et sociaux ont un potentiel important, de même que le renforcement des systèmes de soutien au niveau de la famille et de la collectivité (family and community support systems).

Il convient aussi d'avoir une stratégie de prévention secondaire, fondée sur l'identification des femmes enceintes à haut risque. Le dépistage précoce par les patientes et les professionnels de signes d'irritabilité utérine contribue à la prévention de naissances prématurées en permettant un prompt traitement à l'aide d'agents tocolytiques.

Les données de la littérature concernant l'efficacité des interventions préventives aux stades préconceptionnel et prénatal sont citées.

Zusammenfassung

Niedriges Geburtsgewicht und Frühgeburt: die Bedeutung der Prävention

Der vorliegende Artikel stellt die Situation in den Vereinigten Staaten für den europäischen Leser dar. Obschon die Risiken der Mutter während der Schwangerschaft und des Neugeborenen in den Vereinigten Staaten oft bedrohlicher sind, sind die zugrunde liegenden Probleme und die Folgen doch überall sichtbar.

Die hohen Kosten der entsprechenden Pathologie, vor allem als neonatale Sterblichkeit, aber auch als kindliche Morbidität und deren medizinische Folgekosten werden betont.

Drei Präventivstrategien werden vorgestellt, welche an ein soziales Verhaltensmodell geknüpft sind. Dieses Modell illustriert die verschiedenen Risikofaktoren für niedriges Geburtsgewicht und Frühgeburt inklusive deren pathophysiologische Ursachen. Zwar wird die Notwendigkeit grundlegender gesellschaftlicher Veränderungen erkannt, die Strategien können aber im Gesundheitswesen begonnen werden. Interdisziplinäre Interventionen schon vor der Konzeption und während der Schwangerschaft werden gefordert. Stress soll reduziert werden, Risikoverhalten, Ernährung sollten verbessert werden; Sozialstellen und Familienplanungsstellen haben hier eine wichtige Rolle zu spielen. Ausserdem muss das System der Unter-

stützung in der Familie und ihrer Umgebung verstärkt werden. Zudem werden Strategien der sekundären Prävention benötigt. Diese gelten zuerst der Identifikation der Schwangeren mit hohem Risiko, Früherkennung der Zeichen erhöhter uteriner Irritabilität durch die Patientinnen oder ihrer Betreuer kann zur Verhinderung der Frühgeburt beitragen und eine rechtzeitige Behandlung mit tokolytischen Substanzen erlauben. Eine Übersicht über die pränatalen und präkonzeptuellen Interventionen und deren Wirksamkeit wird gegeben.

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