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Summary Report

Committee on Nutrition of the Mother and Preschool Child
Food and Nutrition Board
Commission on Life Sciences
National Research Council

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This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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COMMITTEE ON NUTRITION OF THE MOTHER AND PRESCHOOL CHILD

PREFACE

The general objectives of this study were to provide to personnel responsible for maternal and child health care information on certain abuses during pregnancy on health and nutritional status and to make recommendations, wherever possible, on the nutritional management of individuals at risk. Specifically, the study aimed (1) to review and evaluate current research and to develop a state-of-the-art report on the effects of certain abuses during pregnancy; (2) to separate, insofar as possible, the effects of the abused substance per se from those effects that may result from alterations in nutrient utilization; and (3) to recommend interventions that may be feasible and effective.

Accordingly, the Food and Nutrition Board's Committee on Nutrition of the Mother and Preschool Child convened a workshop at which prepared papers were presented on cultural practices that affect nutrient intake, the various forms of vegetarianism, pica, smoking, caffeine and alcohol intake, meganutrient dosage, and over-the-counter drug usage during pregnancy. The papers comprising the proceedings of the workshop are published separately and are available from the National Academy Press.

The committee prepared this summary report of the workshop proceedings to provide succinct information to health care personnel on the significance of certain practices during pregnancy in order that they may identify individuals who may be at risk and provide effective consultation and management. This report is also provided with the workshop proceedings.

CONTENTS

SUBCULTURAL PRENATAL DIETS OF AMERICANS

Nearly all societies believe that what a mother eats during pregnancy affects both her health and that of her unborn child. In the hope of exerting some control over the processes of reproduction, societies over the years have developed rules that specify the appropriate diet for reproducing women. The overt purposes of these proscriptive diets are intended to be beneficent: to maintain the health and comfort of the mother, to ensure an easy delivery, and to protect the unborn child. In practice, however, such diets may have risk as well as benefit.

The cultural heterogeneity of the United States is expressed, among other ways, in diet, including prenatal diet. Diets reflect the cultural and historical context in which they arose. An alternative diet is defined here as any diet used by an identifiable group of people larger than a family. The term, therefore, includes not only so-called ethnic diets and what were formerly known as "food fads" (as, for example, vegetarianism) but also the orthodox middle-class American diet and variations of it.

All diets display an internal logic that encompasses and is expressed through food beliefs, patterns of food selection and combination, and knowledge of foods in relation to promoting health and in preventing or treating sickness. Beliefs and expectations that influence food-related behavior penetrate deeply into the fabric of the individual's and community life, so that diet has a large emotional impact and serves an important function in social bonding. For these reasons it is difficult to change (even part of) diets unless the logic behind the modification can be appreciated by those who are being encouraged to change.

Subcultural (Alternative) Diets

The orthodox middle-class American diet generally advocated by health care professionals is a variant of the

diet consumed by affluent groups worldwide. Most users believe that a "good" diet is achieved by eating a variety of foods selected to provide a balance of nutrients.

Despite the fact that it is common, the orthodox diet is but one among many diets consumed by Americans. Other subcultural diets--e.g., "health," vegetarian, Puerto Rican, Mexican American, black American, Asian American--share some or only a few of the characteristics and assumptions of the orthodox diet. For example, few subcultural dietaries emphasize dairy products. Meat, too, may be deemphasized in favor of corn, rice, or vegetables.

The idea that a good diet derives from balancing nutrients is not necessarily current among all Americans, either. Many Hispanic Americans strive to consume a variety of foodstuffs but select foods so as to achieve a balance of "hot" and "cold." In this system foods and medicines have inherent symbolic temperatures; health is maintained through a careful balancing of intake. Thus the pregnant woman, who is "hot," avoids excessively "hot" and excessively "cold" foods in order to stay well. Many poorer Americans, black and white, seek variety and believe health is maintained through balance but follow a set of cultural rules such that balance is attained through a judicious choice of "strengthening" and "heavy" and "light" foods. In this context, "heavy" and "light" represent inherent symbolic characteristics of foods; to some extent, "heavy" coincides with high-calorie. Strengthening foods are more often defined as vegetables than as meats. Some black Americans may believe that a healthy body displays a balance of hot and cold, which can be measured in terms of the quality of the blood. "Excess blood" or "high blood" (high blood pressure) is signified by unusual heat; treatment involves increased use of astringent and acidic (often sodium-rich) foods and decreased use of meats and high-calorie foods.

Thus, when health practitioners make dietary recommendations based on the orthodox model and in the absence of knowledge of a patient's food beliefs and expectations, the therapeutic communication may fail completely, sometimes to the physical detriment of the patient.

Part of the communication problem may reflect semantic differences in the interpretations of such words as "hot," "heavy," "strong," and "energy." Such differences often result in consumption of unusual types and combinations of foods. These variations may be disturbing to orthodox health professionals even though they are of profound

significance for the pregnant woman within her particular sociologic setting.

Beliefs, Avoidances, Cravings, and Aversions

Among numerous beliefs recorded about prenatal diet, the idea that the mother can mark her child before birth apparently is widely held by women of all ages, ethnic groups, and income and education levels. Overuse of a craved food during pregnancy is thought to explain physical or behavioral peculiarities of the infant. More often, unsatisfied cravings are thought to explain birthmarks that mimic the shape of the desired food (such as strawberry- or drumstick-shaped marks). Behavioral markings also can be thought to be advantageous; that is, the mother's consumption of many foods can cause the child to like such foods also.

Another important group of beliefs concerns dietary means by which the mother can ensure an easier delivery. Most important of these, from the biomedical viewpoint, are beliefs that lead a woman to avoid animal-protein foods or to avoid "excessive" weight gain. Most lay people know very well that a smaller weight gain during pregnancy produces a smaller fetus, and most lay people want the mother to have an easy delivery and feel that the child can grow after birth, "catching up" if necessary.

Food avoidances are those foods that the mother consciously chooses not to consume during her pregnancy, usually for a reason she can articulate and that has cogency in her view. The four most commonly avoided foods are sources of animal protein: milk, lean meats, pork, and liver.

Cravings and aversions are powerful urges toward or away from foods, including foods about which the women experience no unusual attitudes outside of pregnancy. The most commonly reported craved foods are sweet foods and dairy foods. The most common aversions are reported to be alcohol, caffeinated drinks, and meats. However, cravings and aversions are not limited to any particular foods or food groups.

Nutritional Significance of Beliefs, Avoidances, Cravings, and Aversions

Information about beliefs, avoidances, cravings, and aversions has often been collected in an anecdotal, censo-

rious, or one-sided manner. Thus, there is detailed information on dietary alterations that appear to be detrimental but little knowledge of total subcultural prenatal dietary intakes. As a result it is difficult to quantify the nutritional effect of restrictive beliefs, avoidances, cravings, or aversions. The nutritional importance of such practices cannot be assessed without reference to the rest of the individual's diet.

Nutritionally, most cravings result in increased intake of calcium and energy, while aversions often result in decreased intake of alcohol and caffeine but also decreased intake of animal proteins. Cravings and aversions are not necessarily deleterious.

Orthodox Prenatal Diet and Problems of Compliance

Several components of the orthodox prenatal diet can be expected to conflict with the dietary habits and ideals of many Americans. In most cases recognition of the differences coupled with simple dietary modifications will allow the health practitioner to make recommendations that are mutually acceptable.

For example, use of dairy products is generally low among black, Asian, and Hispanic Americans. Many are lactose intolerant; others simply are unaccustomed to drinking milk. Health practitioners need to accept these problems as real and to consider the option of recommending alternative sources of calcium. Emphasis on meat and eggs also is often troubling not only because these foods tend to be expensive but also more importantly because animal proteins are the focus of many aversions and avoidances. Alternative dietary recommendations, such as mixtures of vegetable proteins, to provide high-quality protein would be appropriate.

Awareness of alternative dietary practices in pregnancy is of practical importance in the risk assessment and surveillance as well as the dietary counseling of all pregnant women. The practices, and the belief and value systems that support them, may be based on convictions at least as strong as those of orthodox nutritionists, and, unless an empathetic, nonjudgmental dialogue can be established, the presence and extent of the practice may not be appreciated. Only through evaluation of the total diet, not just that related to a particular food preference or avoidance, can the nutritional impact of the practice be identified. And only through such a communicative process

will it be possible to identify preventive or therapeutic approaches that will be compatible with both the best scientific information regarding successful pregnancy outcome and the pregnant woman's personal food preferences and value systems. A prudent approach to counseling the pregnant woman who is not an adherent of orthodox middle-class American values is to encourage the use of foods that serve the nutritional needs of the woman, whatever these foods may be.

VEGETARIAN DIETS

Vegetarians need assistance to ensure that their diets are adequate during pregnancy. Because their diets are different, usual advice designed for omnivores is of little help and special guidance may be necessary.

Diet Assessment and Groups at Risk

Vegetarian diets differ greatly in their nutritional characteristics. For this reason it is important to know exactly what the pregnant woman is eating and what nutritional supplements, if any, the woman may be using.

The type, amount, and frequency of animal food consumption is important to determine, since it has a major influence on nutrient intakes. Most American vegetarians follow lacto-ovo (consumption of only milk products and eggs) or lacto (milk products only) vegetarian patterns. A smaller minority consume vegan-like diets, which include either no animal foods at all or only very small amounts of animal foods eaten as condiments or on an infrequent basis.

It is also helpful to determine if additional constraints or preferences with respect to menu selection exist. Vegetarians such as vegans and lacto-vegetarians with far-reaching animal-food avoidances often avoid food items they regard to be "processed," "refined," or "non-organically grown." Instead, they emphasize the use of "natural," "unrefined," "unprocessed," "organically grown," or "health" foods. It is important to determine what these consumption practices are, because in many cases they are unlikely to be amenable to change. Therefore, they must be respected if realistic dietary advice is to be given that the pregnant vegetarian woman is likely to follow.

The use of, or willingness to use, vitamin or mineral supplements also is important to determine, especially if the woman follows a very restrictive diet of a lacto-vegetarian or vegan type involving additional proscriptions, such as those mentioned above.

Membership in certain religious, quasi-religious, or philosophical groups often greatly influences not only dietary practices but other lifestyle-related behaviors (such as alcohol, tobacco, and coffee use) of importance to health and the utilization of health care services. Therefore, these characteristics should be ascertained. Some of these practices are positive from the standpoint of health promotion during pregnancy, while other practices are negative or make counseling more difficult. For example, members of the Seventh-Day Adventist faith follow a lacto-ovo vegetarian diet, do not smoke or use alcoholic beverages, generally understand the basics of planning nutritionally well balanced diets, are willing to use fortified foods or nutrient supplements, seek regular health care supervision when they are pregnant, and adhere to recommendations made by health care professionals. Other groups may present more problems. For example, Hare Krishnas, macrobiotic adherents, and some members of Yogic groups often are reluctant to use nutrient supplements, refuse to submit to certain medical procedures, may be leery of usual health supervision, and may rely on homeopathic remedies and lay healers. Generalization is hazardous since even within these groups diet and other health-related practices are far from homogeneous. However, the diets and lifestyle practices of lacto-ovo vegetarians who belong to traditional vegetarian groups, such as the Seventh-Day Adventist faith, appear to pose fewer risks than do those following diets of a vegan type or other vegetarian diets with extensive food avoidance and loose involvement with the health care system. Adolescents who follow such regimes are at special risk.

Energy and Specific Nutrients

Energy Intakes

Vegans and those who adhere to some of the "new" vegetarian diets often have low energy intakes and consequently low prepregnancy weight, or low pregnancy weight gains. Suggestions of high-energy, high-density foods can be helpful in increasing energy intakes, so that

weight gains are more reasonable and lactation performance is not compromised.

Protein

When energy intakes are adequate, protein intakes are usually satisfactory on most American vegetarian regimens, provided that a variety of foods high in plant protein and at least some animal protein are consumed. Dietary recommendations of complementary proteins are usually sufficient to ensure protein quality if energy needs are met. Protein supplements are unnecessary.

Calcium

Because lacto and lacto-ovo vegetarians often use more milk products than do nonvegetarians, calcium intakes are rarely a problem. Vegans and other vegetarians who avoid milk products entirely or consume them only rarely are likely to have low intakes, and calcium bioavailability may be compromised owing to high phytate or fiber intakes. Calcium-fortified soy milk and alternative calcium sources should be stressed.

Vitamin D

Nutritional osteomalacia is virtually nonexistent among vegetarian and vegan women living in this country, although vitamin D intakes may be lower than usual for omnivores, especially among vegans.

Iron

The usual problems of iron nutriture seen among all pregnant women are present among vegetarians also. Therefore, supplemental iron is recommended.

Vitamin B-12

Intakes of this vitamin are usually sufficient among vegetarians but may be low among vegans. Vitamin B-12-fortified soy products, nutritional yeasts, or vitamin sup-

plements are suggested to supplement the diets of vegans. Fermented soy products are less reliable sources of the vitamin, although they do make some contribution.

Other Vitamins and Minerals

Vegetarians, especially vegans who do not follow diets that have been carefully planned from the nutritional standpoint, may have low intakes of several other micronutrients, although frank deficiencies are rarely reported. Supplementation with vitamin or mineral preparations other than vitamin B-12 and iron is not mandatory but may be advisable in specific cases, such as vegans.

Other Orally Ingested Substances

Most vegetarians avoid excessive amounts of alcohol, tobacco, large amounts of coffee, and over-the-counter or illicit drugs, so that these substances generally pose little risk to them during pregnancy. However, the use of "health" foods or homeopathic remedies in lieu of nutrient supplements and medical attention should be discouraged.

Conclusion

The pregnant vegetarian woman's diet presents special challenges in constructing a nutritional care plan but none that are so unsurmountable that adequacy of intakes other than iron cannot be achieved by dietary means. Vegans require a source of vitamin B-12 as well as iron.

PICA

Pica denotes the compulsion for persistent ingestion of unsuitable substances having little or no nutritional value. Pica of pregnancy is most often reported as consumption of dirt and clay (geophagia) or starch (amylophagia). However, compulsive ingestion of a variety of nonfood substances has been noted, e.g., ice (pagophagia), burnt matches (cautopyreiophagia), hair (trichophagia), stone or gravel (lithophagia), charcoal, soot, toilet-bowl air fresheners, cigarette ashes, mothballs, antacid tab-

lets, milk of magnesia, baking soda, coffee grounds, and even tire inner tubes.

Pica is not new, nor is it limited to any one geographic area, race, creed, culture, sex, or status within a culture. However, it has yet to receive the attention that it deserves for its nutritional and medical implications.

Prevalence of Pica in Pregnancy

Surveys in the southern United States provided some of the first data to identify current pica practices. A study in 1950 indicated that 41 percent of 331 black pregnant women in rural Mississippi ate starch and 27 percent ate clay. Of 30 Caucasians interviewed, 10 and 7 percent reported starch and clay eating, respectively. A 1959 survey of 86 patients in an Alabama hospital showed that clay eating was reported by 49 percent, starch by 27 percent, and both substances by 7 percent. In some studies as many as 75 percent of women attending southern health department clinics consumed starch and 50 percent consumed clay.

Pica practice has been documented in other areas of the United States also. Although it appears to be more common among pregnant black women, it is reported to occur among other ethnic groups.

Medical Implications

The medical implications of pica are not well understood, although certain possibilities are suggestive. On the one hand, the displacement effect of pica substances could result in inadequate dietary intakes of essential nutrients. On the other hand, substances that provide calories (e.g., starch) could contribute to obesity if ingested in amounts above the usual dietary intakes. Some pica substances may contain toxic compounds or quantities of nutrients not tolerated in certain disease states. Some pica substances have a cation exchange capacity and interfere with the absorption of certain mineral elements.

The few studies that included biochemical data yielded mixed findings on the association between pica and nutritional status values. Low hemoglobin levels and frank anemia have been reported in some studies of pregnant women who practiced pica as compared with a comparable

nonpica group. In some cases, higher incidences of toxemia of pregnancy and hypertension have been reported.

Other less frequently reported complications of pica include congenital lead poisoning secondary to maternal pica for wall plaster and a tender, irritable uterus with dystocia associated with fecal impaction from clay ingestion. Two cases of fetal hemolytic anemia have been reported to be due to maternal pica of toilet-bowl air fresheners and moth balls.

Hypothesis of Etiology

A few studies have suggested that pica can be cured in anemic women and children who ingest pica substances by the administration of iron and subsequent maintenance of normal hemoglobin levels. It is not clear, however, if pica per se causes anemia through interference with iron absorption or utilization or by displacing iron-containing foods in the diet. Because there is no consistently observed relationship between pica and iron deficiency, the causes and mechanisms of various pica practices are still obscure.

Health care practitioners must be aware that pica is not uncommon among pregnant women, particularly among low-income black women of rural southern heritage. Because few women volunteer information on pica practices, health care professionals should be alert to the possible effects of pica on dietary adequacy and health.

CAFFEINE

Caffeine is found in coffee, tea, cocoa, chocolate, cola and some other soft drinks, and some drugs. Concern about caffeine's use during pregnancy is based on several known factors. Caffeine is an active central nervous system stimulant, has a drug-like effect, and crosses the placenta to reach the fetus.

Two related methylxanthines, theobromine and theophylline, also have pharmacological effects and reach the fetus. These two compounds have been linked with fetal edema in experimental animals.

Data from a few epidemiological studies of caffeine intake in human pregnancy are available, but the results are inconclusive, mostly because of incomplete information concerning one or more of the following important

variables: the amount and length of caffeine consumption, alcohol intake, smoking habits, age at pregnancy, outcome of prior pregnancies, medications, and illnesses during pregnancy. The best and most recent study to date suggests that caffeine may pose no significant risks when other confounding variables are controlled.*

Animal Studies

Several studies of pregnant animals have suggested that caffeine is associated with birth defects and prenatal toxicity. One of the first such studies, published in 1964, correlated caffeine with prenatal toxicity and cleft palates in mice. Dose-related increases in embryolethality in rats were reported the following year. Observations of cleft palates were also reported in caffeine-treated mice in 1969 and in coffee-treated rats in 1978. Digital defects, especially incomplete or missing digits, were reported in mice in 1965 and in rats and rabbits in 1970. Although several studies of mice showed no digital defects as a result of intakes of 50-75 mg of caffeine per kilogram of body weight, one multigeneration study done in mice produced digital defects after intakes of as little as 12-18 mg/kg.

One of the most recent studies involving caffeine in pregnant rats was conducted by the U.S. Food and Drug Administration (FDA). Caffeine in distilled water was intubated once each day to rats at dose levels of 6, 12, 40, 80, or 125 mg/kg of body weight throughout gestation. Six dams died at 125 mg/kg. Some litters were resorbed in animals fed the two highest levels (80 and 125 mg/kg). Surviving fetuses were lighter and shorter; sternebrae were less ossified or missing; other skull, trunk, and limb bones also were less ossified; and ectrodactyly appeared.

Teratogenic effects were observed only in fetuses of the 80 and 125 mg/kg groups. Abnormalities included hypoplastic nails or missing digits and limb, skull, and

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*The following report was published six months after the workshop was held: Linn, S., S. C. Schoenbaum, R. R. Monson, B. Rosner, P. G. Stubblefield, and K. J. Ryan. 1982. No association between coffee consumption and adverse outcomes of pregnancy. N. Engl. J. Med. 306: 141-145.

trunk hemorrhages. No abnormalities occurred among fetuses of animals fed the lower levels of caffeine.

Implications in Health Practice

Although the human implications of the latest FDA study on rats are unknown, the commissioner of the FDA, in a press statement on September 4, 1980, advised pregnant women to avoid caffeine-containing foods and drugs or to use them sparingly. Following the press statement, steps were taken to communicate the concerns about caffeine to health care professionals, organizations, and centers. In addition, it was proposed that caffeine be removed from the list of compounds generally regarded as safe (GRAS) and placed in an interim status pending further studies.

The Committee on Nutrition of the Mother and Preschool Child agrees that there are insufficient data available to allow quantitative recommendations regarding caffeine intake during pregnancy. This includes the absence of data in evidence for dose-dependent effects or of a threshold dose effect. However, as in other areas of uncertainty, the committee recommends moderation in caffeine intake during pregnancy.

ALCOHOL

Ethanol is one of the oldest and most often abused drugs known to man. Although historical reviews suggest that concern about adverse effects of ethanol on the fetus were voiced hundreds of years ago, recognition of these effects is of relatively recent origin.

Fetal Alcohol Syndrome

Fetal alcohol syndrome (FAS) is a pattern of altered growth and development and occurs in varying degrees in a high percentage of infants born to chronic alcoholic mothers. FAS is characterized by four general categories of abnormality:

- Characteristic facial appearance: broad, flat midface; broad, low nasal bridge with epicanthal folds; a short upturned nose; a relatively long philtrum and narrow

vermilion border of the lips; and relatively narrow palpebral fissures, which in some cases are associated with small or malformed eyes.

- Prenatal growth deficiency: resulting in low birth weight and reduced linear growth and weight gain thereafter.
- Impaired central nervous system performance: including mental retardation or lesser central nervous system effects, such as early developmental delay, tremulousness, hyperactivity, short attention span, and electroencephalographic alterations. Other functional abnormalities, including neonatal hypertonia, hyperacusis, and feeding difficulties during the first year of life, have been observed.
- Increased frequency of major anomalies: including mild cardiac defects (small ventricular or atrial septal defects), occasional serious cyanotic congenital heart lesions, cleft palate, ocular abnormalities (microphthalmos, coloboma of the iris or retina, and optic nerve hypoplasia), axial skeletal defects, renal and genital anomalies, and such positional limb deformities as club foot and dislocated hip.

Epidemiological Studies

Epidemiological studies indicate that the association between maternal alcohol intake and adverse outcome of pregnancy is strongest among severe chronic alcoholic women and suggest that infants of such women are at high risk for serious congenital abnormalities. Recent studies provide evidence that approximately 10 percent of women who consume as little as 1-2 oz. of absolute alcohol or its equivalent per day during the earliest part of pregnancy produce infants with recognizable alterations of growth and/or morphogenesis. More limited evidence suggests that some degree of growth and neurological impairment may persist into later life, although truly long-term evaluations have not yet been reported.

It is not clear at this time whether the pattern of maternal drinking represents an additional risk factor. Adverse effects have been observed in some offspring of women who indulged in "binge" drinking during pregnancy even though "average" intake of alcohol was not sufficiently high to warrant classification of these women in the high-risk category.

Although many of the clinical characteristics of FAS appear to be unique to alcohol, possible contributions by confounding factors, such as malnutrition, have not been clearly delineated. For this reason studies of animals have been made in an attempt to isolate the two effects of the factors.

Animal Studies

In an attempt to control for the caloric but nonnutritive content of alcohol, recent studies have involved administration of alcohol to pregnant animals in either a liquid diet or by intragastric intubation. Control groups were pair-fed isocaloric liquid diets or intubated with isocaloric solutions. The "empty" calories supplied by alcohol were replaced by isocaloric substitution with sucrose, dextrose, or maltose. The results of these studies, including nutritional control groups and an oral route of alcohol administration in their design, demonstrated adverse effects of maternal alcohol ingestion on fetal and neonatal weight and morphological development, as well as on subsequent behavior of the offspring and on brain development and function.

For example, results from studies in rats and mice demonstrated that both acute and chronic alcohol consumption during pregnancy resulted in decreased birth weight and retarded morphological development of the progeny. Moreover, the effect was dose related and more pronounced with exposure during the third trimester of gestation. Alterations in postnatal behavior related to prenatal alcohol exposure also have been demonstrated in rats. Behavioral deficits may be related to abnormal brain morphology, especially in the hippocampus, where abnormal mossy fibers have been reported as a consequence of *in utero* alcohol exposure.

In these studies the role of nutrition was minimized by using appropriate nutritional control groups. This is not to say that nutrition is without effect. The issue of alcohol and nutrition is a complex one that becomes more complicated when pregnancy is an additional variable. Chronic alcohol consumption by pregnant rats results in decreased food intake, which compromises adequate nutrient intake. A further confounding factor is that alcohol may interfere with the absorption of essential nutrients; this factor cannot be controlled by pair-feeding procedures. Thus, even though diets were

fortified with additional protein, vitamins, and minerals, the pregnant animals fed diets containing alcohol or intubated with alcohol solutions may not utilize the nutrients and calories adequately. Alcohol consumption by pregnant dams also influences fetal nutrition by decreasing amino acid transport across the placenta and, possibly, by reducing the supply of folate or zinc to the developing fetus.

It is thus reasonable to propose that nutritional variables associated with chronic alcohol ingestion interact with the direct and/or indirect effects of ethanol to influence adversely the development of the offspring. Whether nutritional deficiencies coupled with alcohol intake exacerbate the effects seen with alcohol alone remains to be determined.

Implications in Health Care

These epidemiological and experimental findings have important implications for clinicians and other health care providers. It is imperative that physicians who care for pregnant or potentially pregnant women recognize that alcohol is a dangerous drug not only for mothers but also for their babies. Thus, a careful history of maternal alcohol intake should be a part of every prenatal evaluation. Mothers should be cautioned against excessive alcohol consumption at any time during pregnancy and those who are found to be drinking heavily should be warned of the risks to their infants.

Secondly, if current trends in social drinking continue, this problem may become more frequent in the future as an increasing number of young women and children are exposed to alcohol. Thus, an important mode of controlling this avoidable tragedy would seem to be the early education of school-age children with regard to the hazards of alcohol and other dangerous drugs.

Finally, it is important for pediatricians to appreciate that FAS may be one of the most frequently recognizable causes of mental deficiency and developmental delay. The identification of affected children has several potential advantages, including the more appropriate use of medical facilities in the evaluation of problems of growth and development, the early recognition of infants at high risk for serious congenital anomalies, and the recognition of a mother at substantial risk for problems in future offspring. Whether the developmental problems identified

in such children might be amenable to early treatment is still unknown.

Although infrequent or modest alcohol ingestion may not constitute a hazard to the fetus, there are insufficient data to quantify "infrequent" and "modest" in terms of specific recommendations. Therefore, because a "safe" level of alcohol intake for pregnant women has not been established, the prudent recommendation is to advise against alcohol intake during pregnancy.

SMOKING

Smoking during pregnancy can affect the mother, the embryo and the fetus, the placenta, and the newborn infant and child. Women who smoke usually have a lower prepregnancy weight, lower weight gain during pregnancy, and lower long-term weight gain. These weight differences are minimized when women abstain from smoking between pregnancies and are exaggerated when nonsmokers take up the habit.

Smoking is one of the most important preventable determinants of low birth weight in the United States.

Maternal Complications

Maternal complications of pregnancy that show a greater incidence among women who smoke cigarettes include placenta previa, abruptio placentae, amnionitis, vaginal bleeding during pregnancy, and possibly premature rupture of the membranes. Lifetime smoking also affects the occurrence of placenta previa, abruptio placentae, and bleeding during pregnancy. These complications appear to increase as the number of cigarettes smoked increases and are 25 percent greater among women who smoke less than one pack per day than among nonsmokers and 92 percent greater among those who smoke more than one pack per day. The risk of spontaneous abortion is 30-70 percent higher among smokers than among nonsmokers.

Effects on Infant

Maternal smoking has an adverse effect on birth weight. Infants of smoking mothers weigh on the average 200 g less than babies born to mothers who do not smoke; the decrement in birth weight is proportional to the number

of cigarettes smoked. The placental ratio (placental weight to fetal weight) is higher for the gestations of women who smoke. This increase results from a decreased newborn birth weight and from a slight increase in absolute placental weight in heavy smokers.

Children of women who smoke during and after pregnancy experience higher rates of morbidity and mortality up to 5 years of age. Some studies suggest that older children of mothers who smoke have slight but measurable deficits in physical growth, intellectual ability, emotional development, and behavior. These effects are seen in women of all races and transcend educational level, occupation, and income. The effects of smoking, however, are additive to such risk factors as low prepregnancy weight, developmental prematurity, and poverty.

Many of these smoking effects follow a dose-response relationship up to the three-pack-a-day level of smoking. The neonates of smoking mothers tend to have elevated hemoglobin levels and comparably elevated hematocrit levels in proportion to the extent of maternal cigarette utilization during pregnancy. The elevation of these two hematologic measures indicates the response of the fetal blood-forming tissues to the products of smoking during pregnancy.

The smoking effect is also shown in an increased number of low Apgar scores in the neonate, both with respect to the 1-minute and the 5-minute Apgar scores and using various cutoff values (7, 5, 3, and 2). This effect on the Apgar scores persists even after exclusion of the prematurely born. Cigarette smoking during pregnancy also manifests itself in an excess of low Bayley developmental test scores at 8 months, both for the Bayley "mental" items and the Bayley "motor" items. Since low Bayley test scores are predictive of low Binet and Wechsler IQ scores, the early effects of cigarette smoking during pregnancy may relate to test scores in the early school years.

Mechanisms of the Smoking Effect

Clues to the mechanisms by which smoking may increase the risk of pregnancy complications are available from pathological and physiological studies of maternal organs, the placenta, fetal organs, and serum levels of substances important for cell and tissue integrity.

Tobacco smoke contains more than 2000 compounds, including nicotine, carbon monoxide, oxides of nitrogen,

ammonia, polycyclic aromatic hydrocarbons, hydrogen cyanide, and vinyl chloride. Of these, the most significant with respect to the pregnant woman and the fetus appear to be nicotine, carbon monoxide, and the polycyclic aromatic hydrocarbons. Experimental studies with rats and rabbits indicate that exposure of pregnant animals to tobacco smoke leads to a reduction in birth weight of the offspring. Female rats exposed to cigarette smoke show an increased incidence of sterility, resorption of the fetuses *in utero*, abortions, and newborn deaths as compared with controls. Although food intake is decreased somewhat in pregnant animals exposed to smoke, experiments with pair-fed controls indicate that reduction in fetal weight is independent of maternal food intake.

Nicotine concentrations in the serum of pregnant smokers range from 14 to 41 ng/ml, the exact concentration varying in relation to filter type, the amount smoked, puff frequency and volume, and other factors. Nicotine rapidly crosses the placenta. Administration of nicotine to mature rats causes a rise in blood pressure, bradycardia, and hypoxia. Nicotine causes a decrease in placental amino acid transport. This effect may be mediated through an increase in acetylcholine release from placental villi and may account for fetal growth retardation.

Carbon monoxide increases carboxy hemoglobin concentrations 4-5 percent per pack of cigarettes smoked per day. Although carbon monoxide diffuses across the placenta relatively slowly, fetal carboxyhemoglobin concentrations are somewhat higher than those of the mother. Exposure of dams to carbon monoxide during gestation results in decreased fetal weights and increased perinatal mortality. Prenatal carbon monoxide exposure also may have long-term effects on the central nervous system of the offspring.

Polycyclic aromatic hydrocarbons such as benzo[*a*]pyrene concentrate in the placenta and to a lesser extent in the fetus, suggesting that the placenta may protect the fetus from these substances. These compounds are potent carcinogens, and mouse fetuses injected *in utero* with benzo[*a*]pyrene late in gestation have an increased incidence of lung, liver, and mammary neoplasms. Although the genetic risk to human beings is unknown, it has been shown that male cigarette smokers may have an increased number of abnormal spermatozoa and that both paternal and maternal chromosomal aberrations may be increased in smokers.

Other components of cigarette smoke, such as cyanide and cadmium, are known to be increased in body fluids and tissues of smokers and may have an adverse effect on infant growth and increased perinatal mortality.

Hypothesis for the Effects of Maternal Smoking on the Fetus and Newborn Infant

Because cigarette smoke contains many chemicals, many of which are toxic, no single factor can be implicated in the adverse effects on the mother or the infant. The two substances that have been most commonly implicated and that have been most studied are nicotine and carbon monoxide. Both of these compounds may exert their effects through a common pathway: tissue hypoxia. Nicotine-induced hypoxia may occur rather rapidly following smoking of a cigarette by a pregnant mother. Carbon monoxide-mediated hypoxia probably develops more slowly but may persist for a longer period of time. Thus, the two compounds may act together to maintain the fetus in a chronic state of hypoxia. Interactions with other factors also may adversely affect the fetus. Other such factors may be inadequate maternal nutrition; maternal anemia; exposure to carbon monoxide; or exposure to alcohol, caffeine, and various drugs.

OVER-THE-COUNTER DRUGS

Currently, there are about 500,000 over-the-counter (OTC) drugs on the market. These drugs include the nonnarcotic analgesics (such as aspirin), cough and cold remedies, sedatives, stimulants, laxatives and antidiarrheal agents, antacids, weight-reducing agents, and nutrient supplements.

Surveys of OTC drug use have shown the intake of at least one such drug by approximately 65 percent of pregnant women. Drug groups most commonly used are nonnarcotic analgesics and nutrient supplements.

Some of these drugs can cause adverse outcomes of pregnancy in experimental animals. Others are strongly implicated as teratogens. There are, however, considerable difficulties in attempting to link the use of OTC drugs with adverse pregnancy outcome in humans. One such difficulty is that of separating the effect of the illness for which the drug was taken from the effects of the

drug itself. In addition, women who take such drugs tend to have a higher incidence of other self-abusive behaviors, such as consumption of alcohol and megadoses of nutrients.

In pregnant rodents, aspirin (salicylates) produces malformations, especially of the skeleton. The doses used in animal studies have been higher than those usually consumed by pregnant women. However, malformations have been described in infants born to mothers who ingested large amounts of aspirin, and it has been suggested that the ingestion of 650 mg, four times a day during the first trimester, may result in congenital defects. In contrast to this suggestion, the U.S. Collaborative Perinatal Study of the National Institutes of Health found no evidence that aspirin consumption was associated with congenital abnormalities in a prospective study of 50,000 pregnancies.

An additional concern about aspirin consumption during pregnancy is that it has been implicated in the syndrome of persistent pulmonary hypertension in neonates, perhaps by causing premature closure of the ductus arteriosus. Aspirin also displaces bilirubin from its binding to albumin, thereby increasing the amount of free bilirubin that can pass to the fetal brain and cause kernicterus. A dose-dependent increase in the incidence of stillbirths has also been noted, although this could have been related to the medical condition for which the aspirin was taken or to other maternal self-abusive behaviors.

Salicylamide, the amide derivative of salicylic acid, is a component of many OTC drugs. In animal studies, salicylamide produces teratogenic effects when given early in gestation and impaired skeletal maturation and calcium deposition if given in late gestation. To date, no such effects have been observed in the progeny of women taking drugs containing salicylamide.

Acetaminophen, a compound of some OTC analgesics, produces loss of appetite, poor efficiency of food utilization, low weight gain, alopecia, and skeletal abnormalities in the fetuses of pregnant animals. Similar effects in pregnant women have not yet been recorded.

Adverse effects of other commonly used OTC drugs, such as antacids and cough medicines, have not been sufficiently investigated. Reported associations between the use of such drugs and developmental abnormalities may result from other self-abusive behaviors of pregnant women or the underlying conditions for which the drugs were used as a therapy.

Further studies of the relationship between the use of OTC drugs (particularly nonnarcotic analgesics) and pregnancy outcomes are recommended, including methodology to examine temporal and dose relationships. Until more definitive data are available, the indiscriminate use of OTC drugs during pregnancy should be discouraged.

NOTE:

Physicians' Desk Reference--Over-the-Counter Drugs

For many years, Medical Economics has published a volume called the Physicians' Desk Reference (PDR). This volume contains detailed listings by therapeutic indication as well as by manufacturer of various prescription drugs available in the United States and Canada. There is also a section that describes each product by color, so that identification of an unknown drug is possible. PDR now has published a smaller edition that lists OTC drugs. This provides the clinician with a ready reference for the composition, indications, and contraindications of most of the commonly used OTC drugs.

MEGADOSE NUTRIENTS

The term "megadose" is used to indicate intakes of nutrients in amounts of 10 or more times the recommended dietary allowances (RDA). At these levels, some nutrients may become toxic to the fetus.

Several unique features of the maternal-fetal relationship theoretically could predispose to fetal toxicity from maternal ingestion of excessive levels of essential nutrients. As a general rule, susceptibility to damage is greater during development, i.e., early pregnancy rather than after developmental processes are complete. Moreover, the placenta transports many substances from mother to fetus against a concentration gradient, which means that the fetus may be exposed to unusually high nutrient levels with maternal overdosage. Finally, the fetus has a limited capacity for the excretion of potentially toxic compounds.

A detailed review of available literature indicates that some potential exists for fetal toxicity with maternal overdosage of five essential nutrients--two fat-soluble vitamins (vitamins A and D), two water-soluble vitamins (ascorbic acid and vitamin B-6), and one mineral

(iodine). The evidence is strongest with respect to vitamin A, which has been demonstrated to be teratogenic in a variety of animal species when consumed at 100 or more times its known requirements. The reported human experience is limited to three individual case reports. Urinary tract abnormalities were observed in the newborn infant of one woman who took 40,000 IU daily between the sixth and tenth weeks of gestation and in one who ingested 25,000 IU daily in the first trimester and 50,000 IU daily thereafter. In the third case, a woman who consumed 150,000 IU daily from day 19 to day 60 of gestation produced an infant with central nervous system defects.

Large doses of vitamin D given to rabbits have produced hypercalcemia, aortic lesions, and other malformations. A possible association between maternal vitamin D overdosage and infantile hypercalcemia with attendant facial abnormalities, growth retardation, and aortic stenosis was suggested by the increased frequency with which this condition occurred at the time of widespread fortification of milk and milk products in Great Britain. The American Academy of Pediatrics advises that vitamin D intake should not exceed 400 IU per day. Treatment of pregnant hypoparathyroid women with 50,000 to 100,000 IU per day has failed to produce neonatal abnormalities in such patients. However, there is considerable doubt that normal healthy women can safely consume doses of that magnitude.

A suggestion that chronic ascorbic acid overdosage during pregnancy might predispose to infantile scurvy comes from anecdotal reports in humans and from experiments in guinea pigs. It has also been suggested that excessive intake of vitamin B-6 during pregnancy might produce a pyridoxine-dependency state in the newborn, although fairly extensive observations in the human and in certain animal species have failed to confirm this relationship.

Very high intakes of iodine, ingested as expectorants in the treatment of asthma or other respiratory conditions, have produced congenital goiter in the newborn. Intake levels were 500-1000 times the RDA of 175 µg/day. Congenital goiter has been described with intakes of 12 mg/day, but this level of intake from dietary sources is unlikely unless such sources as kelp tablets (10-20 tablets per day) are taken with iodized salt and prenatal mineral supplements that contain iodine.