FOHS Week 6 Seminar assignment.   Due Feb. 12, 2008:

Read the attached articles (The NY Times article, the Teratology position statement, and pages 5-15 in the MMWR). Come to seminar prepared to discuss the following questions (you may need to do some additional research on your own). At then end of seminar you will hand in your prep notes and/or responses to these questions.

1. Has folic acid supplementation of flour reduced neurological birth defects? If so, where and by how much?

2. Should the level of folic acid supplementation be increased, left the same, reduced, or eliminated altogether?

3. How is folic acid supplementation similar to or different from supplementation with Niacin, Riboflavin, Vitamin D, Vitamin A, and/or iron?

4. Generally, mandatory enrichment of food staples like flour and milk are public health measures to prevent illness. Is this a good thing or a bad thing? Where should we draw the line? At at what economic cost? At what human cost? Is there a better way to achieve the same goals?

The New York Times
nytimes.com
December 4, 2007

ESSAY

A Growing Debate Over Folic Acid in Flour

By DARSHAK M. SANGHAVI, M.D.

Every year, an estimated 200,000 children around the world are born with crippling defects of the spinal column. Many are paralyzed or permanently impaired by spina bifida; some, with a condition called anencephaly (literally, "no brain"), survive in a vegetative state.

It is a stubborn and terrible problem, in the developed and developing worlds alike. But many experts believe it could be greatly eased by a simple government measure: requiring that flour be fortified with the dietary supplement folic acid, which has been shown to prevent these neural tube defects if taken by expectant mothers from before conception through the first trimester.

The debate over folic acid is a familiar one, and Americans could be excused for thinking it was over. Since 1998, the federal government has required that almost all flour be fortified with the supplement.

But in fact, the requirement has meant women receive an average extra dose of just 100 micrograms of folic acid a day — far below the levels that have been shown in studies to prevent spina bifida and other neural tube defects. For more than a decade, the Food and Drug Administration has resisted calls to require that the amount be doubled.

To Dr. Godfrey Oakley, the former director of birth defects research for the Centers for Disease Control and Prevention, it is a baffling situation. "Until this day the F.D.A. still obstructs folic acid supplementation," he said. "It's like making a vaccine against polio with only one strain instead of four."

The debate is intensifying. In the past two years, the American Medical Association, the March of Dimes and several pediatric societies have called on the food and drug agency to reconsider. The only country now adding the amount recommended by experts like Dr. Michael Katz, the medical director of the March of Dimes, is Chile.

Folic acid's promise emerged 40 years ago, when British obstetricians realized that spina bifida often occurred when mothers had a form of anemia caused by folic acid deficiency. Then, in a 1991 British study of mothers of children with spina bifida, Dr. Nicholas Wald, the lead investigator, found such extraordinary results that he stopped the trial prematurely. When the women took folic acid daily before their next conception and through the first trimester of pregnancy, spina bifida recurrences fell 72 percent.

"That was the most important scientific data I'd heard in my career," Dr. Oakley said.

In 1992, the Public Health Service called for all menstruating women to take a daily folic acid pill. (Folic acid helps only if taken before the fetus's nervous system forms, which is before women realize they're pregnant.)

But when few women followed that advice, the C.D.C. prevailed on the food and drug agency to hold hearings on folic acid fortification. That led to the federal requirement in effect today, though the food and drug agency was never enthusiastic about it. Dr. David A. Kessler, the food and drug commissioner at the time, told me recently that the issue "was probably the hardest decision I had on my tenure on the commission."

"Adding a biologically active ingredient to the food supply of 300 million people is a very weighty issue," Dr. Kessler said. "You can't experiment on the American people."

For critics of the idea, the first problem was that the recommended doses of folic acid were large, dwarfing the amount found in the average person's diet. The second worry was that too much folic acid could mask symptoms of vitamin B12 deficiency and perhaps lead to irreversible brain damage in older people.

More recently, some researchers have pointed out that the rate of colon cancer rose slightly in the late 1990s, after the folic acid requirement took effect. But colon cancer rates have since fallen, suggesting the increase was a statistical anomaly.

Skeptics remain. Dr. James Mills, a foe of increased fortification at the National Institutes of Health, concludes that most women's folate levels are already high enough to avoid preventable neural tube defects. He says there is no way the population's safety can be guaranteed with higher fortification levels, and asks, "How would you design a study to determine if this is safe?"

Yet the folic acid requirement has had clear benefits. Within a year of the limited fortification, the C.D.C. reported, neural tube defect rates fell 20 percent, and no reports of widespread toxic effects emerged.

And there is good reason to think that requiring more fortification may prevent more birth defects. Blood levels of folate among women have been declining, according to a C.D.C. study released last January, perhaps because of worsening obesity and the popularity of low-carbohydrate diets.

The United States has a long history of accepting food fortification for public health. Iodine in salt has been shown to prevent many cases of mental retardation; while almost one-third of the world's population has no access to iodized salt, Americans have been ingesting it since 1924. Similarly, additives like vitamin D in milk to prevent rickets, iron in flour to prevent anemia and fluoride in water to prevent cavities have been widespread in the developed world for half a century. Ultimately every public health intervention, including fortification, widespread vaccination and banning trans fats, involves a leap of faith, since no study can ever prove safety beyond the shadow of a doubt. One can show only that unintended harm is very unlikely.

From this perspective, the fact that 300 million Americans have already been exposed to folic acid in flour constitutes one of the world's largest medical trials — one that suggests fortification is safe. And new benefits have emerged: in June, the American Heart Association reported that folic acid prevented common birth defects of the heart, and the journal Lancet reported that more folic acid might reduce strokes in adults by 18 percent.

Ideally, the authorities would address every concern before any intervention. But this approach causes public health paralysis.

Dr. Oakley bemoans the lack of incentives to prevent birth defects. For example, efforts to include package inserts in tampons or oral contraceptives to educate women about folic acid have not been adopted.

By comparison, he pointed to the introduction of a new vaccine two decades ago that led to the near eradication of Hemophilus meningitis in children.

"The vaccine-industrial complex works like a charm," Dr. Oakley said. But with folic acid, things are slow: "Nobody's making any money off this."

Darshak Sanghavi is a pediatric cardiologist at the University of Massachusetts Medical School and the author of "A Map of the Child: A Pediatrician's Tour of the Body."

Teratology Society Consensus Statement on Use of Folic Acid to Reduce the Risk of Birth Defects

Neural tube defects are common and severe birth defects that include the fatal condition anencephaly and the disabling condition spina bifida. Recent randomized controlled studies, (Crandall et al., '95; Czeizel and Dudas, '92; MRC Vitamin Study Research Group, '91) have shown that women who consume folic acid-containing supplements, while eating their usual diets, have 50–75% fewer infants with neural tube defects. Neural tube defects develop within the first month after conception. Maternal use of folic acid after this point in pregnancy cannot influence the development of spina bifida. Because many pregnancies are unplanned and pregnancy is often not diagnosed until after the time that neural tube defects have developed in a fetus, the diets of all women who are capable of having children should be enriched in folic acid.

No adverse effect has been reported with taking supplemental folic acid during pregnancy. It has been suggested that folic acid fortification of staple foods may delay the diagnosis of pernicious anemia in older individuals, but we believe that this theoretical risk is clearly outweighed by the demonstrable benefit of fortification.

The mechanism by which folic acid acts to reduce the risk of birth defects is unknown. Research designed to understand this mechanism and whether other metabolically related chemicals are as effective as folic acid offers the hope of preventing more birth defects.

The Teratology Society, therefore, recommends that 1) women in the childbearing age group take a daily vitamin supplement containing 0.4 mg of folic acid; 2) fortification of enriched cereal grain products be carried out to a level that will provide 0.4 mg of folic acid each day to at least 95% of women in the reproductive age group; and 3) research designed to understand the mechanism by which folic acid or metabolically related chemicals reduce the risk of birth defects be strongly encouraged.

LITERATURE CITED

Crandall, B.F., V.L. Corson, J.D. Goldberg, G. Knight, and I.S. Salafsky (1995) Folic acid and pregnancy. Am. J. Med. Genet., *55:*134–135.

Czeizel, A.E., and I. Dudas (1992) Prevention of the first occurrence of neural tube defects by periconceptional vitamin supplementation. N. Engl. J. Med., *327:*1832–1835.

MRC Vitamin Study Research Group (1991) Prevention of neural tube defects: Results of the MRC Vitamin Study. Lancet, *338:*132–137.

This consensus statement was written for the Teratology Society Public Affairs Committee by Dr. Lewis Holmes, Dr. John Harris, Dr. Godfrey P. Oakley, Jr., and Dr. J.M. Friedman. The statement has been approved by the full Public Affairs Committee and by the Council of the Teratology Society.

CDC

MMWR

Morbidity and Mortality Weekly Report

www.cdc.gov/mmwr

Weekly January 11, 2008 / Vol. 57 / No. 1

National Birth Defects Prevention Month and Folic Acid Awareness Week

January is National Birth Defects Prevention Month. Birth defects affect approximately one in 33 newborns and are a leading cause of infant mortality in the United States (*1*). The cost of lifetime care for infants born in a single year with one or more of 17 severe birth defects was estimated at $6 billion in the most recent study (*1*).

This year, National Birth Defects Prevention Month focuses on preventing infections during pregnancy. Health-care professionals should encourage women who are pregnant or who might become pregnant to adopt behaviors that can prevent infections that might cause birth defects. For example, women can reduce their risk for cytomegalovirus infection by washing their hands often, especially after changing diapers, and by not sharing food, drinks, or eating utensils with young children. Additional information about preventing infections during pregnancy is available at http://www.cdc.gov/ncbddd/pregnancy_gateway/infection.htm.

January 7–13 is National Folic Acid Awareness Week. Health-care professionals should encourage every woman who might become pregnant to consume 400 μg of synthetic folic acid every day in a vitamin supplement or in foods enriched with folic acid. Following this regimen before and during early pregnancy can prevent serious birth defects of the spine and brain (*2*). Additional information about CDC's birth defects prevention activities is available at http://www.cdc.gov/ncbddd.

References

1. CDC. Economic costs of birth defects and cerebral palsy—United States, 1992. MMWR 1995;44:694–9.
2. CDC. Recommendation for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. MMWR 1992;41(No. RR-14).

Update on Overall Prevalence of Major Birth Defects — Atlanta, Georgia, 1978–2005

Major structural or genetic birth defects affect approximately 3% of births in the United States, are a major contributor to infant mortality (*1,2*), and result in billions of dollars in costs for care (*3*). Although the causes of most major birth defects are unknown, concerns have been raised that certain factors, such as an increase in the prevalence of diabetes among women, might result in increased prevalence of birth defects over time (*4*). This report updates previously published data from the Metropolitan Atlanta Congenital Defects Program (MACDP), the oldest population-based birth defects surveillance system in the United States with active case ascertainment (*5*). For the period 1978–2005, CDC assessed the overall prevalence of major birth defects and their frequency relative to selected maternal and infant characteristics. The MACDP results indicated that the prevalence of major birth defects

INSIDE

MMWR QuickGuide

Recommended Immunization Schedules for Persons Aged 0–18 Years — United States, 2008

department of health and human services
Centers for Disease Control and Prevention

The *MMWR* series of publications is published by the Coordinating Center for Health Information and Service, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30333.

Suggested Citation: Centers for Disease Control and Prevention. [Article title]. MMWR 2008;57:[inclusive page numbers].

in metropolitan Atlanta, Georgia, remained stable during 1978–2005 but varied by maternal age and race/ethnicity, birthweight, and gestational age. Tracking the overall prevalence of major birth defects can identify subgroups that are affected disproportionately; additional measures focused on these subgroups might improve preconception care and care during pregnancy to prevent birth defects.

State-based surveillance programs monitor the prevalence of certain birth defects through various methods, including passive hospital-based reporting and active medical-record abstraction (*6*). These data are used for prevention, education, policy, and health-care planning (*7*). However, most state-based surveillance programs were established in recent years and only monitor certain types of defects; therefore, population-based estimates of the overall prevalence of all defects and data on long-term trends are lacking in the United States. MACDP, established in 1967 by CDC, Emory University, and the Georgia Mental Health Institute, monitors the prevalence of all major structural or genetic defects at the time of delivery among live births, stillbirths, and pregnancies electively terminated after prenatal diagnosis of defects at ≥20 weeks' gestation in the five central counties of metropolitan Atlanta (*5*). MACDP defines major structural or genetic birth defects as conditions that 1) result from a malformation, deformation, or disruption in one or more parts of the body, a chromosomal abnormality, or a known clinical syndrome; 2) are present at birth; and 3) have a serious, adverse effect on health, development, or functional ability.

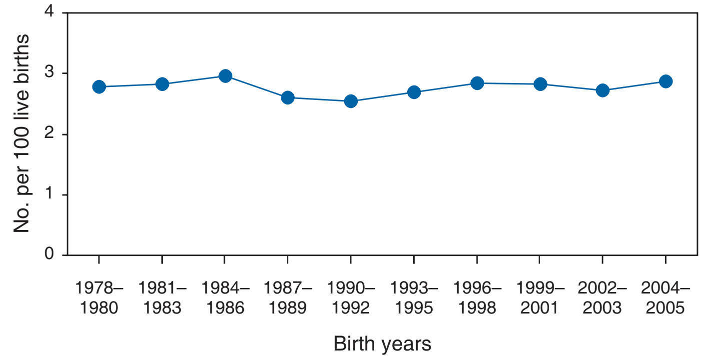
To collect data on birth defects, trained MACDP records abstractors visit birth and pediatric hospitals and genetic laboratories to review in-patient medical records of infants and fetuses of ≥20 weeks' gestation. Systematic case-finding by the abstractors at each hospital includes review of labor and delivery logs, nursery and intensive-care logs (including neonatal intensive-care logs), stillbirth and pathology logs, and disease indices. The medical records for each infant or fetus with a potential birth defect are then examined to identify those with defects that meet the MACDP case definition. Information about identified defects among live births is updated until age 6 years. However, the system might miss certain defects, including those that 1) occur among children whose families move away from the Atlanta area before diagnosis, 2) are managed on an outpatient basis only, 3) are unrecognized among stillbirths, or 4) are diagnosed prenatally among pregnancies subsequently terminated outside a hospital setting. Denominator data on the number of live births to residents of the five counties are obtained from vital records of the Georgia Department of Human Resources. Such data have included maternal Hispanic ethnicity only since 1990. Data on birthweight have been available since 1978 for the offspring of white mothers and black mothers and since 1997 for Hispanic mothers; data on gestational age have been available since 1988 for the offspring of white mothers and black mothers and since 1997 for Hispanic mothers.

For MACDP purposes, prevalence is defined as the number of infants and fetuses with a major birth defect that were delivered during a specified period divided by the number of live births during that period. For this report, the overall prevalence of major defects per 100 live births was estimated for each of three periods (1978–1987, 1988–1996, and 1997–2005) and by the following characteristics: maternal race/ethnicity (white, black, or Hispanic), maternal age (<35 years or ≥35 years), infant birthweight (<2,500 g or ≥2,500 g), gestational age (20–36 weeks or ≥37 weeks), and sex. The three periods were chosen because they corresponded to available denominator data for birthweight and gestational age and enabled comparisons of periods of approximately equal length. Data for 2005 are preliminary because abstractions for defects that were not diagnosed or did not require hospitalization until the child was several months of age might not yet have been processed. Data for racial/ethnic groups other than whites, blacks, and Hispanics were not included in this report because of small numbers. Prevalence ratios (PRs) and 95% confidence intervals (CIs) were calculated. Trend over time in overall prevalence was evaluated using the Mantel-Haenszel test for trend.

The overall prevalence of major defects was stable from 1978 (2.8 per 100 live births) to 2005 (3.0 per 100) (test for trend p = 0.19) (Figure). During this period, the number of births in the metropolitan Atlanta area more than doubled, from 24,396 in 1978 to 51,400 in 2005. Prevalence of defects generally was lower among births to black mothers (PR = 0.94, CI = 0.93–0.95) and Hispanic mothers (PR = 0.89, CI = 0.86–0.93) than to white mothers.

Births to women aged ≥35 years had a greater prevalence of defects than births to women aged <35 years (PR = 1.28, CI = 1.24–1.31), with this excess prevalence increasing over time (Table). During 1978–2005, the overall prevalence was greater among infants with birthweight <2,500 g (PR = 2.97, CI = 2.90–3.04) and among infants with gestational age of 20–36 weeks (PR = 2.53, CI = 2.47–2.59). Prevalence was greater among males than among females (PR = 1.17, CI = 1.16–1.18); however, the higher prevalence among males decreased when defects that occur almost exclusively in males (e.g., hypospadias) were excluded (PR = 1.04, CI = 1.02–1.05).

FIGURE. Overall prevalence of major structural or genetic birth defects,* by selected maternal and infant characteristics and maternal race/ethnicity — Metropolitan Atlanta Congenital Defects Program (MACDP), 1978–2005†



* MACDP defines major structural or genetic birth defects as conditions that 1) result from a malformation, deformation, or disruption in one or more parts of the body, a chromosomal abnormality, or a known clinical syndrome; 2) are present at birth; and 3) have a serious, adverse effect on health, development, or functional ability.

† 2005 data are preliminary. Mantel-Haenszel test for trend, p = 0.19.

Reported by: *L Rynn, J Cragan, MD, A Correa, MD, PhD, Div of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, CDC.*

Editorial Note: The findings in this report indicate that the overall prevalence of major birth defects in metropolitan Atlanta did not change significantly during 1978–2005. This finding suggests that, over time, no changes occurred in major risk factors that affect birth defects overall. This information can be useful in assessing the success of prevention interventions for defects overall.

However, although the overall prevalence did not change significantly, a greater prevalence of birth defects among infants of low birthweight and preterm gestation might signal a need for increased prenatal health care and planning for the extended-care requirements. The greater prevalence of defects among the offspring of women aged ≥35 years likely reflects an upward trend in maternal age distribution and the progressive association of certain defects as maternal age increases beyond 35 years (*8,9*). The lower prevalence of defects among black and Hispanic infants might reflect an actual lower prevalence among these groups; however, racial and ethnic variation in health-insurance coverage, diagnosis of nonsymptomatic defects through pediatric and subspecialty care, and ascertainment of these defects by MACDP's hospital-based methods also might affect differences in defect prevalence. Further evaluation of these differences is needed.

The stable overall prevalence of major birth defects in Atlanta is consistent with the trend observed for many individual defects (*5*). However, the prevalence of certain

TABLE. Overall number and prevalence* of major structural or genetic birth defects,[†] by selected maternal and infant characteristics and maternal race/ethnicity — Metropolitan Atlanta Congenital Defects Program (MACDP), 1978–2005[§]

		Maternal race/ethnicity									
		White		Black		Hispanic[¶]		Total**			
Characteristic	Period	No.	Prevalence	No.	Prevalence	No.	Prevalence	No.	Prevalence	Prevalence ratio	(95% CI[††])
Total		**15,448**	**2.92**	**10,971**	**2.62**	**2,224**	**2.57**	**29,769**	**2.76**	—	—
Age of mother (yrs)											
<35	1978–1987	4,141	2.69	3,007	2.97	—	—	**7,554**	**2.80**	Referent	—
≥35		371	2.94	117	3.66	—	—	**572**	**3.19**	1.14	(1.05–1.23)
<35	1988–1996	4,366	2.81	3,021	2.31	293	2.25	**7,953**	**2.47**	Referent	—
≥35		878	3.35	349	3.15	28	2.64	**1,305**	**3.27**	1.24	(1.18–1.31)
<35	1997–2005	3,949	3.00	3,622	2.43	1,703	2.55	**9,793**	**2.64**	Referent	—
≥35		1,432	3.70	783	3.70	193	3.37	**2,540**	**3.62**	1.31	(1.26–1.35)[§§]
Birthweight (g)[¶¶]											
≥2,500	1978–1987	3,825	2.30	2,224	2.40	—	—	**6,168**	**2.34**	Referent	—
<2,500		944	9.04	958	7.21	—	—	**1,935**	**8.05**	3.02	(2.90–3.15)
≥2,500	1988–1996	4,297	2.33	2,213	1.78	—	—	**7,003**	**2.19**	Referent	—
<2,500		927	8.42	1,150	6.42	—	—	**2,225**	**7.48**	2.98	(2.87–3.10)
≥2,500	1997–2004	3,868	2.71	2,608	1.97	1,237	2.12	**8,131**	**2.29**	Referent	—
<2,500		918	9.21	1,243	6.68	342	9.50	**2,631**	**7.69**	2.93	(2.83–3.04)
Gestational age (wks)* **											
≥37	1988–1996	4,141	2.40	2,304	2.00	—	—	**6,937**	**2.33**	Referent	—
20–36		990	7.26	998	4.94	—	—	**2,137**	**6.14**	2.33	(2.25–2.42)
≥37	1997–2005	4,043	2.62	2,973	2.02	1,433	2.14	**8,963**	**2.29**	Referent	—
20–36		1,217	7.60	1,357	5.95	424	7.57	**3,141**	**7.12**	2.68	(2.60-2.77)
Sex											
Female	1978–1987	1,933	2.25	1,422	2.72	—	—	**3,416**	**2.43**	Referent	—
Male		2,857	3.13	1,753	3.26	—	—	**4,700**	**3.18**	1.13	(1.11–1.16)
Female	1988–1996	2,003	2.26	1,386	1.98	145	2.10	**3,663**	**2.14**	Referent	—
Male		3,241	3.48	1,971	2.74	176	2.44	**5,580**	**3.12**	1.19	(1.17–1.21)
Female	1997–2005	2,148	2.58	1,795	2.14	855	2.40	**5,050**	**2.33**	Referent	—
Male		3,244	3.73	2,609	3.01	1,043	2.83	**7,294**	**3.25**	1.17	(1.15–1.18)

* Per 100 live births.
† MACDP defines major structural or genetic birth defects as conditions that 1) result from a malformation, deformation, or disruption in one or more parts of the body, a chromosomal abnormality, or a known clinical syndrome; 2) are present at birth; and 3) have a serious, adverse effect on health, development, or functional ability.
§ 2005 data are preliminary.
¶ Data on age of mother and sex of offspring have been available by maternal Hispanic ethnicity only since 1990. Data on birthweight and gestational age of offspring have been available by maternal Hispanic ethnicity only since 1997. Mothers categorized as Hispanic might be of any race.
** Includes racial/ethnic populations other than white, black, and Hispanic.
†† Confidence interval.
§§ Trend in major defect prevalence over time is statistically significant (p<0.05) using Mantel-Haenszel test for trend.
¶¶ 2005 birthweight data were not available.
*** Data on gestational age were available for the offspring of white mothers and black mothers only since 1988.

defects in Atlanta has changed over time. For example, a decline in the prevalence of anencephaly and spina bifida might reflect fortification of the U.S. grain supply with folic acid and increased consumption of folic acid vitamin supplements. Progressive declines in the prevalence of clubfoot not associated with spina bifida and of cleft lip (with or without cleft palate) also have been observed. In contrast, the prevalence of Down syndrome and other autosomal trisomies among the offspring of mothers aged ≥35 years has increased over time, likely reflecting the increase in age distribution of mothers aged ≥35 years in metropolitan Atlanta (CDC, unpublished data, 2007). The prevalence of ventricular septal defect, atrial septal defect, and valvar pulmonic stenosis also have increased progressively, likely reflecting increased use of bedside echocardiography to diagnose heart defects among newborns (*5*).

The findings in this report are subject to at least four limitations. First, because childbearing women in Atlanta might differ from women in other areas of the United States with respect to characteristics that might be associated with the risk for birth defects, the observed prevalence of major birth defects in metropolitan Atlanta might not be generalizable to other populations. Second, the specific defect inclusion and exclusion criteria used by MACDP might differ from those used by other surveillance programs, resulting in differences in prevalence estimates (*10*). For example, the MACDP case definition does not include developmental, functional, or other types of congenital disorders (e.g., nonstructural or genetic disorders not detected in children aged ≤6 years). Third, data in this report do not include defects diagnosed prenatally among pregnancies electively terminated before 20 weeks' gestation or outside a hospital setting. Failure to ascertain these pregnancies might result in underestimation of the prevalence of major defects (*9*). Finally, data on age of mother and sex of offspring were available by maternal Hispanic ethnicity only since 1990, and data on birthweight and gestational age of offspring were available by maternal Hispanic ethnicity only since 1997.

Population-based data on the overall prevalence of major birth defects can be used to identify subgroups that are affected disproportionately, evaluate prevention measures (e.g., promotion of preconception health and health care use), and recommend additional health-care services and resources where needed. These Atlanta findings should encourage surveillance programs elsewhere to monitor the overall prevalence of major defects in their areas, assess their public health burden, and examine the variability of defects among specific populations.

Acknowledgments

This report is based, in part, on contributions by J Kucik, C Alverson, S Gilboa, D Gambrell, and MACDP abstractors and staff members, Div Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, CDC.

References

1. Hoyert DL, Mathews TJ, Menacker F, et al. Annual summary of vital statistics: 2004. Pediatrics 2006;117:168–83.
2. Yoon PW, Olney RS, Khoury MJ, Sappenfield WM, Chavez GF, Taylor D. Contributions of birth defects and genetic diseases to pediatric hospitalizations: a population-based study. Arch Pediatr Adolesc Med 1997;151:1096–103.
3. CDC. Hospital stays, hospital charges, and in-hospital deaths among infants with selected birth defects—United States, 2003. MMWR 2007;56:25–9.
4. Yang J, Cummings EA, O'Connell C, Jangaard K. Fetal and neonatal outcomes of diabetic pregnancies. Obstet Gynecol 2006;108(3 pt 1): 644–50.
5. Correa A, Cragan JD, Kucik ME, et al. Metropolitan Atlanta Congenital Defects Program: 40th anniversary edition surveillance report. Reporting birth defects surveillance data 1968–2003. Birth Defects Res A Clin Mol Teratol 2007;79:65–186.
6. National Center on Birth Defects and Developmental Disabilities, CDC. State birth defects surveillance program directory. Birth Defects Res Part A Clin Mol Teratol 2006;76:837–93.
7. Williams LJ, Mai CT, Edmonds LD, et al. Prevalence of spina bifida and anencephaly during the transition to mandatory folic acid fortification in the United States. Teratol 2002;66:33–9.
8. Hollier LM, Leveno KJ, Kelly MA, McIntire DD, Cunningham FG. Maternal age and malformations in singleton births. Obstet Gynecol 2000;96(5 pt 1):701–6.
9. Siffel C, Correa A, Cragan J, Alverson CJ. Prenatal diagnosis, pregnancy terminations and prevalence of Down syndrome in Atlanta. Birth Defects Res A Clin Mol Teratol 2004;70:565–71.
10. Holmes LB. Need for inclusion and exclusion criteria for the structural abnormalities recorded in children born from exposed pregnancies. Teratol 1999;59:1–2.

Use of Supplements Containing Folic Acid Among Women of Childbearing Age — United States, 2007

Neural tube defects (NTDs) are serious birth defects of the brain (anencephaly) and spine (spina bifida) that affect approximately 3,000 pregnancies each year in the United States (*1*). In 1992, the U.S. Public Health Service recommended that all women of childbearing age in the United States capable of becoming pregnant consume 400 μg of folic acid daily to reduce their risk for having a pregnancy affected by NTDs (*2*). To assess awareness, knowledge, and behavior related to folic acid among women of childbearing age (aged 18–45 years), CDC analyzed the results of a national survey conducted annually by the Gallup Organization during the period 2003–2007.* This report summarizes the results of that analysis, which indicated that, among all women of childbearing age, those aged 18–24 years had the least awareness regarding folic acid consumption (61%), the least knowledge regarding when folic acid should be taken (6%), and the lowest reported daily use of supplements containing folic acid (30%). Because women in this age group account for nearly one third of all births in the United States (*3*), promotion of folic acid consumption should be targeted to this population.

Since 1995, the March of Dimes Foundation has contracted the Gallup Organization to conduct a series of national, random-digit–dialed telephone surveys of a proportionate stratified sample of women of childbearing age to assess awareness, knowledge, and behavior regarding folic acid. The surveys include multiple-choice and open-ended questions. To assess awareness of folic acid, respondents were asked a multiple-choice question, "Have you ever heard, read, or seen anything about folic acid?" To assess knowledge about folic acid, respondents were asked two open-ended questions, "What have you heard, read, or seen about folic acid?" and "Which vitamins or mineral supplements do you think are important to women of childbearing age?" To assess the source of knowledge about folic acid, respondents were asked an open-ended question, "Where did you learn about folic acid?" To assess behavior, respondents were asked an open-ended question, "What type of vitamin or mineral supplements do you take on a daily basis?" Women who reported taking a daily multivitamin, a prenatal vitamin, or a folic acid only supplement were considered to be taking a supplement containing folic acid. To assess barriers

* The 2006 survey included only women aged 18–35 years and therefore was excluded.

to taking folic acid, respondents were asked an open-ended question, "Why do you not take any vitamin or mineral supplement on a daily basis?" Women who are currently pregnant were not excluded from the sample. For certain survey questions, stratification by pregnancy status provided useful comparative information. In 2007, a total of 2,003 women of childbearing age (18–45 years) were sampled, with women aged 18–24 years being oversampled. The response rate was 32%. Statistical estimates were weighted to reflect the total population of women aged 18–45 years in the contiguous United States who resided in households with telephones. For total results based on this sample of women, the error attributable to sampling was plus or minus 2 or 3 percentage points (with 95% confidence).

In 2007, approximately 40% of all women surveyed reported daily consumption of a supplement containing folic acid. This percentage is equal to that observed in 2004 and is an increase from 33% in 2005 and from 32% in 2003. Women who were nonwhite, were aged 18–24 years, had less than a high school education, or had a household income of <$25,000 were the least likely to report daily consumption of a supplement containing folic acid (Table 1).

Several differences in folic acid awareness and knowledge were observed among age groups. In 2007, approximately 61% of women aged 18–24 years reported being aware of folic acid, compared with 87% of women aged 25–34 years and 89% of women aged 35–45 years (Table 2). Additionally, women aged 18–24 years were less knowledgeable about the need for folic acid consumption before pregnancy (6%), compared with women aged 35–45 years (16%). In 2007, approximately 42% of women surveyed reported folic acid as the most important vitamin for women of childbearing age. This represented an increase from 30% in 2005. However, differences were observed by age group, with women aged 25–34 years being most likely to mention folic acid (55%), compared with women aged 35–45 years (43%) and women aged 18–24 years (20%).

In 2007, approximately 33% of women who were aware of folic acid reported that they had heard about folic acid from their health-care provider, followed by a magazine or newspaper (31%) and radio or television (23%). Women aged 18–24 years were more likely to hear about folic acid from a magazine or newspaper (25%) or school or college (22%) than from their health-care provider (17%), whereas 37% of women aged 25–34 years and 36% of women aged 35–45 years reported hearing about folic acid from their health-care provider.

Reported daily consumption of a supplement containing folic acid also differed by age group. In 2007, women aged 25–34 years were the most likely to report consuming a daily supplement containing folic acid (47%), followed by women aged 35–45 years (40%) and women aged 18–24 years (30%). Among women who reported not taking a vitamin or mineral supplement on a daily basis, the most common reason was "forgetting" (33%), followed by "no need" (18%), "no reason" (14%), and "already get balanced nutrition" (12%).

TABLE 1. Percentage of women aged 18–45 years who reported taking a supplement containing folic acid daily,* by survey year and selected sociodemographic characteristics — United States, 2003–2007†

Characteristic	2003 (N = 2,006) (%)	2004 (N = 2,012) (%)	2005 (N = 2,647) (%)	2007 (N = 2,003) (%)
Race				
White	34	43	36	40
Nonwhite	28	31	23	36
Ethnicity				
Hispanic	29	38	27	38
Non-Hispanic	33	40	34	40
Age group (yrs)				
18–24	25	31	24	30
25–34	34	39	36	47
35–45	35	46	37	40
Education				
Less than high school	21	19	20	29
High school	28	32	31	36
College (any)	37	48	35	48
Annual household income				
<$25,000	24	30	27	32
$25,000–$39,999	31	40	28	39
$40,000–$49,999	39	48	37	43
≥$50,000	38	46	38	43
Pregnancy status				
Pregnant	82	81	90	93
Not pregnant	30	37	31	37
Total	**32**	**40**	**33**	**40**

SOURCE: Gallup Organization.

* Based on response to an open-ended question, "What type of vitamin or mineral supplements do you take on a daily basis?"

† Statistical estimates were weighted to reflect the total population of women aged 18–45 years in the contiguous United States who resided in households with telephones. For total results based on this sample of women, the error attributable to sampling was plus or minus 2 or 3 percentage points (with 95% confidence). The 2006 survey included only women aged 18–35 years and therefore was excluded.

Reported by: *JR Petrini, PhD, March of Dimes Foundation, White Plains, New York. HC Hamner, MPH, AL Flores, MPH, J Mulinare, MD, C Prue, PhD, Div of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, CDC.*

Editorial Note: In 1998, the Food and Drug Administration mandated that folic acid be added to cereal grain products. A 26% decline in the NTD rate in the United States was observed from the period before (1995–1996) to the period after (1999–2000) fortification (*1*). However, racial/ethnic disparities persisted, with Hispanic women having

TABLE 2. Percentage of women aged 18–45 years reporting awareness, knowledge, and behavior related to folic acid, by survey year and age group — United States, 2003–2007*

Survey year/ Age group (yrs)	Awareness†	Knowledge§	Behavior¶
2003 (N = 2,006)			
18–24	73	8	25
25–34	82	11	34
35–45	81	10	35
Total	**79**	**10**	**32**
2004 (N = 2,012)			
18–24	70	10	31
25–34	80	14	39
35–45	80	11	46
Total	**77**	**12**	**40**
2005 (N = 2,647)			
18–24	72	5	24
25–34	88	9	36
35–45	87	8	37
Total	**84**	**7**	**33**
2007 (N = 2,003)			
18–24	61	6	30
25–34	87	12	47
35–45	89	16	40
Total	**81**	**12**	**40**

SOURCE: Gallup Organization.

* Statistical estimates were weighted to reflect the total population of women aged 18–45 years in the contiguous United States who resided in households with telephones. For total results based on this sample of women, the error attributable to sampling was plus or minus 2 or 3 percentage points (with 95% confidence). The 2006 survey included only women aged 18–35 years and therefore was excluded.

† Based on response to a multiple-choice question, "Have you ever, heard, read, or seen anything about folic acid?"

§ Based on response to an open-ended question, "What have you heard, read, or seen about folic acid?"

¶ Based on response to an open-ended question, "What type of vitamin or mineral supplements do you take on a daily basis?"

the highest rate of NTDs and the lowest reported consumption of folic acid (*4*). A statewide survey conducted annually in California during the period 2002–2006 indicated that Hispanic women had the lowest use of supplements containing folic acid (*5*). In addition to the racial/ethnic disparities, differences of supplement use by age have been reported (*6*).

Although year-to-year variation has been observed over time, the percentage of women of childbearing age who reported consumption of a daily supplement containing folic acid increased overall from 28% in 1995 to 32% in 2003 (*6*) and to 40% in 2004 and 2007. One of the *Healthy People 2010* objectives is to increase to 80% the proportion of all women of childbearing age who consume 400 μg of folic acid daily to reduce their risk for serious birth defects (objective no. 16-16a) (*7*). Thus, although progress has been made toward this goal, approximately 60% of women of childbearing age surveyed in 2007 were still not consuming a daily supplement containing folic acid. Women aged 18–24 years have the highest rate of unintended pregnancies in the United States (*8*) but remain the least aware of and knowledgeable about folic acid and the least likely to report consuming a supplement containing folic acid. These findings warrant the continued promotion of folic acid consumption among all women of childbearing age and especially among women aged 18–24 years. Folic acid education that promotes consumption of folic acid from various sources (e.g., supplements containing folic acid and fortified foods), in addition to foods rich in folate, can increase the possibility of all women consuming the recommended daily amount of 400 μg (*9*).

The findings in this report are subject to at least two limitations. First, the low response rate of 32% increases the risk that response bias might have affected the results. Results should be interpreted with caution and in the context of other surveys. For certain questions, recall bias also might have affected results. Second, the survey was limited to households with landline telephones, and the results might not be representative of all households. Whether this limitation would result in overestimates or underestimates in various results is not predictable.

The findings in this report indicate that women aged 18–24 years identified schools or colleges and magazines or newspapers as their primary sources for folic acid information, so these two channels might provide important opportunities to reach this population. Research has indicated that women in this age group are more likely to respond to folic acid messages that do not focus on pregnancy or infants (*10*). Innovative and effective messages tailored to women aged 18–24 years are needed to help change behaviors, increase awareness and knowledge regarding folic acid consumption, and ultimately reduce the incidence of NTDs.

References

1. CDC. Spina bifida and anencephaly before and after folic acid mandate—United States, 1995–1996 and 1999–2000. MMWR 2004;52:362–5.
2. CDC. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. MMWR 1992;41(No. RR-14).
3. Martin JA, Hamilton BE, Sutton PD, et al. Births: final data for 2005. Natl Vital Stat Rep 2007;56(6).
4. Williams LJ, Rasmussen SA, Flores A, Kirby RS, Edmonds LD. Decline in the prevalence of spina bifida and anencephaly by race/ethnicity: 1995–2002. Pediatrics 2005;116:580–6.
5. CDC. Trends in folic acid supplement intake among women of reproductive age—California, 2002–2006. MMWR 2007;56:1106–9.
6. Green-Raleigh K, Carter H, Mulinare J, Prue C, Petrini J. Trends in folic acid awareness and behavior in the United States: the Gallup Organization for the March of Dimes Foundation surveys, 1995–2005. Matern Child Health J 2006;10(5 suppl):S177–82.

7. US Department of Health and Human Services. Healthy people 2010 (conference ed, in 2 vols). Washington, DC: US Department of Health and Human Services; 2000. Available at http://www.health.gov/healthypeople.
8. Finer LB, Henshaw SK. Disparities in rates of unintended pregnancy in the United States, 1994 and 2001. Perspect Sex Reprod Health 2006;38:90–6.
9. Institute of Medicine. Dietary reference intake: folate, other B vitamins, and choline. Washington, DC: National Academies Press; 1998.
10. Lindsey LL, Hamner HC, Prue CE, et al. Understanding optimal nutrition among women of childbearing age in the United States and Puerto Rico: employing formative research to lay the foundation for national birth defect prevention campaigns. J Health Commun 2007;12:733–57.

Trends in Wheat-Flour Fortification with Folic Acid and Iron — Worldwide, 2004 and 2007

Consumption of adequate amounts of folic acid by women before pregnancy and during early pregnancy decreases their risk for having a pregnancy affected by neural tube defects (NTDs) (*1*), the most common preventable type of birth defects worldwide. Consumption of iron ameliorates iron deficiency, the most prevalent nutritional deficiency in the world, affecting approximately 2 billion persons (*2*). Although certain populations consume substantial amounts of rice and corn, worldwide, the consumption of wheat flour is greater than that of any other cereal grain. Fortification of wheat flour is an effective, simple, and inexpensive strategy for supplying folic acid, iron, and other vitamins and minerals to large segments of the world population. To assess the global change from 2004 to 2007 in 1) the percentage of wheat flour being fortified with folic acid and iron; 2) the total number of persons overall and women in particular with access to fortified wheat flour; and 3) the total number of newborns whose mothers had access to fortified wheat flour during pregnancy, CDC analyzed data from the Flour Fortification Initiative (FFI).* This report summarizes the results of that assessment, which indicated that the worldwide percentage of wheat-flour fortification increased from 18% in 2004 to 27% in 2007. The estimated number of persons with access to fortified wheat flour increased by approximately 540 million, and the annual number of newborns whose mothers had access to fortified wheat flour during pregnancy increased by approximately 14 million. Nonetheless, approximately two thirds of the world population lacks access to fortified wheat flour. Programs should continue to expand coverage of wheat-flour fortification as a strategy to increase folic acid and iron consumption.

FFI maintains a surveillance system that monitors national fortification practices and policies related to wheat flour processed in roller mills worldwide. FFI staff members use information from food balance sheets from the Food and Agriculture Organization of the United Nations to compile data on the amount (in metric tons) of wheat flour used at the country level.† FFI consultants and staff members visit or communicate with governmental, nongovernmental, or industry representatives involved in wheat production or milling in the various countries to collect country-level data on laws and regulations regarding wheat-flour fortification, annual production of fortified wheat flour, and the type and level of vitamins and minerals used in fortification. Data are collected continuously as laws and regulations change, and the database is updated annually. For this report, CDC used the FFI surveillance system database to document the number of countries with mandatory wheat-flour fortification (i.e., countries with laws or regulations requiring fortification of wheat flour with specific vitamins or minerals and penalties for lack of compliance) and calculated the percentage of wheat flour that is fortified as the amount of fortified wheat flour divided by the total amount of wheat flour used in each country. The results are presented by World Health Organization (WHO) region§ and worldwide. The percentage of persons in each country with access to fortified wheat flour was assumed to be equal to the percentage of wheat flour that is fortified. Multiplying this percentage by data on country population size obtained from the U.S. Central Intelligence Agency and by data on country-level birth rates from the United Nations International Children's Emergency Fund (UNICEF), CDC estimated the total number of persons and the total number of women with access to fortified wheat flour, and the number of newborns whose mothers had access to fortified wheat flour during pregnancy by country. Data were analyzed for 2004 (the year in which FFI was launched) and for November 2007 (the most recent data available).

From 2004 to 2007, the number of countries with documented national regulations for mandatory wheat-flour for-

* FFI is a network of public, private, and civic organizations with the goal of making fortification of wheat flour a standard practice. The FFI goal is for 70% of the wheat flour processed in roller mills (i.e., industrial mills in which flour or meal is produced by crushing grain between rollers) to be fortified with at least folic acid and iron by the end of 2008. Additional information is available at http://www.sph.emory.edu/wheatflour.

† Additional information on food balance sheets is available from the Food and Agriculture Organization of the United Nations at http://www.fao.org/docrep/003/x9892e/x9892e00.htm.

§ A list of countries in each WHO region is available at http://www.who.int/about/structure/en/index.html.

tification increased from 33 to 54. Fifty of the 54 countries with mandatory fortification in 2007 required fortification with both iron and folic acid, two with folic acid but not iron, and two with iron but not folic acid. Twenty-four of those countries also mandated wheat-flour fortification with thiamin, riboflavin, and niacin; two with thiamin and riboflavin; and two with thiamin. The percentage of wheat flour processed in roller mills that was fortified increased from 18% in 2004 to 27% in 2007. Nearly 540 million additional persons, including 167 million additional women aged 15–60 years, had access to fortified wheat flour in 2007 compared with 2004, and the annual number of newborns whose mothers had access to fortified wheat flour during pregnancy increased by approximately 14 million (Table). By region, the greatest increase in the percentage of wheat flour being fortified was in the Eastern Mediterranean Region: from 5% in 2004 to 44% in 2007 (Figure). The portion of wheat flour being fortified increased from 90% to 97% in the Americas Region (the region with the highest percentage of wheat flour being fortified), from 26% to 31% in the African Region, from 16% to 21% in the South-East Asia Region, from 3% to 6% in the European Region, and from 2% to 4% in the Western Pacific Region.

Reported by: *G Maberly, MD, Emory Univ, Atlanta, Georgia. L Grummer-Strawn, PhD, ME Jefferds, PhD, JP Peña-Rosas, MD, MK Serdula, MD, VQ Tyler, MPH, Div of Nutrition, Physical Activity, and Obesity, National Center for Chronic Disease Prevention and Health Promotion; RJ Berry, MD, J Mulinare, MD, Div of Birth Defects and Development Disabilities, National Center for Birth Defects and Development Disabilities; I Parvanta, MS, Office of the Director, Coordinating Center for Health Promotion; NJ Aburto, PhD, EIS Officer, CDC.*

Editorial Note: Previous studies in the United States have established that fortification of wheat flour is cost effective (*3*). The cost of fortification with folic acid and iron is approximately $1.50 U.S. dollars per metric ton of wheat flour, which is pennies per person per year. NTDs affect approximately 200,000 births each year, resulting in the death of fetuses or newborns or in lifelong disabilities that result in tens to hundreds of thousands of dollars per year in direct costs per person. In the United States, folic acid fortification has an estimated economic benefit of $312–$425 million annually. The estimated benefit-cost ratio of U.S. folic acid fortification is 40:1 (*3*). Worldwide, iron deficiency is associated with approximately 861,000 deaths, approximately 35 million disability-adjusted life years lost, and billions of dollars in indirect costs annually (*4*). The benefit-cost ratio for iron fortification is approximately 36:1 (*5*).

Ecological studies from the United States (*6*), Canada (*7*), and Chile (*8*) have documented decreases of 26%, 42%, and 40%, respectively, in the rate of NTD-affected births after implementation of national regulations mandating wheat-flour fortification with folic acid. Investigators in Ireland documented that small increases in red blood cell folate levels reduce the risk for NTDs, indicating that small increases in folic acid consumption might result in substantial reductions in NTD incidence in the population (*9*). No adequate ecological studies have examined the health impact of fortifying wheat flour with iron; however, research trials have demonstrated an association between the consumption of wheat flour fortified with iron and increased hemoglobin levels and decreased prevalence of anemia (*10*).

Successful wheat-flour fortification worldwide requires adoption and enforcement of legislation for mandatory fortification at the national level, and industry and public-sector commitment for

FIGURE. Percentage of wheat flour processed in roller mills that was fortified — worldwide and by World Health Organization (WHO) region, 2004 and 2007

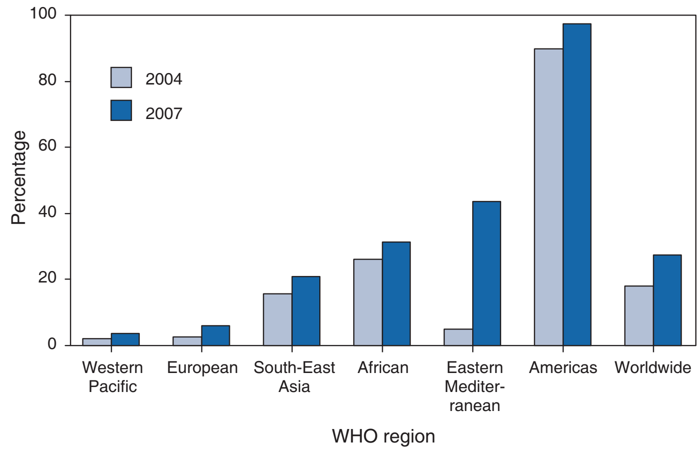


TABLE. Estimated number and percentage of persons and women who had access to fortified wheat flour and of newborns whose mothers had access to fortified wheat flour during pregnancy — worldwide, 2004 and 2007

Category	Total population	2004 No.*	2004 (%)	2007 No.*	2007 (%)	Change from 2004 to 2007 No.	Change from 2004 to 2007 (%)
Total persons	**6,512,822†**	**1,271,363**	**(19.5)**	**1,810,659**	**(27.8)**	**539,297**	**(8.3)**
Women aged 15–60 yrs	**2,142,225†**	410,091	(19.1)	577,461	(27.0)	167,370	(7.8)
Newborns whose mothers had access	**133,804§**	27,052	(20.2)	41,060	(30.7)	14,007	(10.5)

* In thousands. Calculated from data from the Flour Fortification Initiative, available at http://www.sph.emory.edu/wheatflour.
† In thousands, mid-2006 estimate. From U.S. Central Intelligence Agency, available at http://www.cia.gov.
§ In thousands. From United Nations International Children's Emergency Fund (UNICEF) birth rate estimates, available at http://www.unicef.org.

such legislation. Mandatory fortification places the same requirements on all flour producers and is more likely to succeed if the milling industry is well organized and supports fortification (*2*). Concomitant consumer education and social-marketing programs are important to ensure consumer acceptance of fortified flour products. The development and implementation of consumer education and communication strategies that include evidence of the health benefits of fortification require commitment from the public sector and is strengthened by the support of civic organizations. Through public, private, and civic collaboration, advocates and public health agencies are promoting wheat-flour fortification and the fortification of other food items (e.g., other cereal grains, soy and fish sauces, sugar, margarine, and cooking oil) to increase worldwide consumption of vitamins and minerals.

The findings in this report are subject to at least three limitations. First, flour-use data are based on Food and Agriculture Organization estimates, which, in certain instances, can be subject to substantial margins of error and do not account for differing levels of flour use among various subpopulations. However, these are the only standardized data that permit international comparisons. Second, the FFI surveillance system only monitors wheat flour processed in roller mills. The system accounts for the known production of substantial amounts of wheat flour in stone-grinder mills in Pakistan and India and assumes that the amount of flour produced in such mills in other countries is not substantial (V. Tyler, CDC, personal communication, 2008). Finally, the percentage of persons with access to fortified flour was considered to be equal to the percentage of flour that is fortified. The extent to which mandatory fortification regulations are implemented and enforced in each country is not known. In addition, several countries have terminology in their fortification laws that allows certain types of flour (e.g., "not enriched" or "brown" flour) to remain unfortified. These factors might have resulted in overestimates of persons with access to fortified flour and the percentage of flour that is fortified.

Although increases occurred from 2004 to 2007 in the number of newborns whose mothers had access to fortified wheat flour, the total number of women aged 15–60 years who had access, and the total number of persons overall who had access, the majority of the world population still lacks access to fortified wheat flour and to the folic acid, iron, and other vitamins and minerals this flour provides. Wheat-flour fortification remains an important strategy for decreasing vitamin and mineral deficiencies, along with targeted supplementation, mass fortification of other food products, in-home fortification strategies, and integrated health and economic-development programs.

Acknowledgments

This report is based, in part, on the contributions of K Grimm, B Sinclair, N Shinoda, public health students at Emory Univ, Atlanta, GA; and S Alford, MPH, Flour Fortification Initiative.

References

1. Wald NJ, Law MR, Morris JK, Wald DS. Quantifying the effect of folic acid. Lancet 2001;358:2069–73.
2. Allen L, de Benoist B, Dary O, Hurrell R, eds. Guidelines on food fortification with micronutrients. Geneva, Switzerland: World Health Organization; 2006.
3. Grosse SD, Waltzman NJ, Romano PS, Mulinare J. Reevaluating the benefits of folic acid fortification in the United States: economic analysis, regulation, and public health. Am J Pub Health 2005;95:1917–22.
4. Stoltzfus RJ, Mullany L, Black RE. Iron deficiency anemia in comparative quantification of health risks: the global burden of disease due to 25 selected major risk factors. Cambridge, MA: Harvard University Press; 2003.
5. Horton S. The economics of food fortification. J Nutr 2006;136:1068–71.
6. Williams LJ, Mai C, Edmonds LD, et al. Prevalence of spina bifida and anencephaly during the transition to mandatory folic acid fortification in the United States. Teratology 2002;66:33–9.
7. De Wals P, Tairou F, Van Allen M, et al. Reduction in neural-tube defects after folic acid fortification in Canada. New Engl J Med 2007;357:135–42.
8. Hertrampf E, Cortes F. Folic acid fortification of wheat flour: Chile. Nutr Rev 2004;62:S44–8.
9. Daly LE, Mills JL, Molloy A, et al. Minimum effective dose of folic acid for food fortification to prevent neural-tube defects. Lancet 1997;350:1666–9.
10. Sun J, Huang J, Li W, et al. Effects of wheat flour fortified with different iron fortificants on iron status and anemia prevalence in iron-deficient anemic students in Northern China. Asia Pac J Clin Nutr 2007;16:116–21.

Prevalence of Neural Tube Defects and Folic Acid Knowledge and Consumption — Puerto Rico, 1996–2006

Birth defects are one of the leading causes of infant mortality in both the mainland United States (*1*) and Puerto Rico (*2*). Neural tube defects (NTDs) are serious birth defects of the spine and brain; two of the most common NTDs are spina bifida and anencephaly. In the United States, NTD prevalence is higher among Hispanic women than among non-Hispanic white or non-Hispanic black women (*3*). In Puerto Rico, where most residents are Hispanic, the prevalence of NTDs (8.68 per 10,000 live births [*4*]) is higher than in the mainland United States (5.59 [*5*]). Consumption of folic acid before and during early pregnancy can prevent NTDs. To assess trends in NTD prevalence and prevalence of knowledge and consumption of folic acid supplements in Puerto Rico, data were analyzed from the Birth Defects Surveillance System (BDSS) for 1996–2005 and the Behavioral Risk Factor Surveillance System (BRFSS) for 1997–2006. This report describes the results of those analyses, which indicated that prevalence of folic acid knowledge and consumption among women of childbearing age increased from 1997 to 2003 but decreased from 2003 to 2006. During similar periods, NTD prevalence declined from 1996 to 2003 but did not change significantly from 2003 to 2005. To resume the decline in prevalence of NTDs, additional measures might be needed to increase folic acid supplement use among Puerto Rican women of childbearing age.

BDSS is a population-based, active surveillance system that assesses approximately 50,000 births in Puerto Rico each year; the most recent available data are from 2005. BDSS records abstractors conduct weekly visits to all birthing hospitals and read medical logs for neonatal intensive care units, pediatric units, delivery rooms, pathology laboratories, and clinics for infants at high risk. Abstractors also visit clinics for children with special health-care needs and pediatric cardiology offices. BDSS staff members review and code case information and perform annual record cross-checks and linkages with vital statistics databases in Puerto Rico. Data from BDSS and vital statistics records are used to calculate total annual NTD prevalence as the number of spina bifida or anencephaly cases (including live births, fetal deaths, stillbirths, spontaneous abortions, and elective terminations) per year, multiplied by 10,000 and then divided by the number of live births for each year.

BRFSS is an ongoing, random-digit–dialed telephone survey of the noninstitutionalized civilian population aged $\geq$18 years. BRFSS data files are weighted to the respondent's probability of being selected and to the age-, race-, and sex-specific populations from the annually adjusted census for Puerto Rico. To assess folic acid knowledge and daily folic acid consumption among nonpregnant women aged 18–44 years in Puerto Rico, data were collected from the surveys administered in 1997, 1998, 2000, 2002, 2003, 2004, and 2006; no folic acid questions were included in the 1999, 2001, and 2005 surveys. The total number of women surveyed during the 7 years of surveys was 6,356. Consumption was defined as reported daily consumption of a vitamin pill or supplement containing folic acid.* Knowledge was defined as knowing that folic acid consumption is recommended by certain health experts for the prevention of birth defects.† Statistical estimates were weighted to reflect the total population of women aged 18–44 years in Puerto Rico. During 1996–2006, the BRFSS response rate§ in Puerto Rico ranged from 67%–81%, based on Council of American Survey and Research Organizations (CASRO) guidelines. Differences in data points were considered statistically significant at $p<0.05$ by chi-square test.

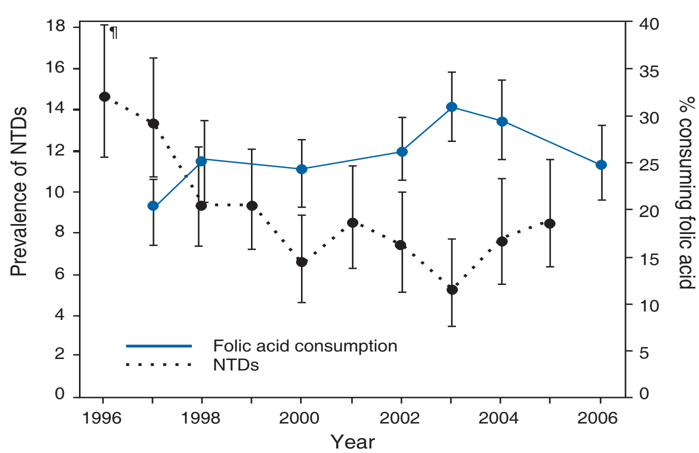
The annual number and prevalence of NTDs (i.e., spina bifida and anencephaly) in Puerto Rico declined significantly ($p<0.05$) from 93 (14.7 per 10,000 live births) in 1996 to 27 (5.3 per 10,000) in 2003 (Figure). From the 2003 levels, the number and prevalence of NTDs did not change significantly in 2004 (40 [7.8 per 10,000]) or 2005 (44 [8.7 per 10,000]). During a similar period, the estimated prevalence of folic acid supplement consumption among nonpregnant women aged 18–44 years increased significantly from 20.2% in 1997 to 30.9% in 2003, then decreased to 24.8% in 2006 (Figure, Table 1). Similarly, the estimated prevalence of knowledge of folic acid increased

* Participants were asked, "Do any of the vitamin pills or supplements you take contain folic acid?" Those who responded "yes" were then asked, "How often do you take this vitamin pill or supplement?"

† Participants were asked, "Some health experts recommend that women take 400 micrograms of the B vitamin folic acid, for which one of the following?" "To make strong bones? To prevent birth defects? To prevent high blood pressure? Some other reason?" Only participants who responded, "To prevent birth defects," were counted as reporting knowledge of folic acid.

§ The percentage of persons who completed interviews among all eligible persons, including those who were not successfully contacted. Additional information is available at http://www.cdc.gov/brfss/technical_infodata/quality.htm.

FIGURE. Prevalence* of neural tube defects (NTDs)† and estimated folic acid consumption§ among nonpregnant women aged 18–44 years — Birth Defects Surveillance System and Behavioral Risk Factor Surveillance System, Puerto Rico, 1996–2005 and 1997–2006



* Per 10,000 live births.
† Anencephaly and spina bifida.
§ Defined as reported daily consumption of a vitamin pill or supplement containing folic acid.
¶ 95% confidence interval.

TABLE 1. Estimated prevalence of folic acid consumption* among nonpregnant women aged 18–44 years, by selected characteristics — Behavioral Risk Factor Surveillance System, Puerto Rico, 1997–2006

	1997 (N = 586)		1998 (N = 677)		2000 (N = 996)		2002 (N = 1,091)		2003 (N = 1,034)		2004 (N = 977)		2006 (N = 995)	
Characteristic†	%	(95% CI§)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
Age group (yrs)														
18–24	16.5	(9.5–23.6)	22.6	(15.3–29.9)	20.8	(13.1–28.3)	18.5	(12.7–24.3)	26.7	(19.3–34.2)	26.9	(18.6–35.3)	20.5¶	(14.1–26.9)
25–34	22.2	(16.6–27.8)	29.6	(23.5–35.7)	25.5	(19.8–31.3)	27.1	(21.2–33.1)	32.5	(25.8–39.2)	30.4	(23.9–36.8)	24.2	(19.0–29.4)
35–44	21.4	(15.5–27.3)	22.9	(17.4–28.5)	26.1	(20.6–31.6)	32.0	(27.1–36.9)	32.3	(27.4–37.2)	30.6	(25.4–35.7)	28.6¶	(24.3–32.8)
Education														
Less than high school graduate	10.5	(3.9–17.0)	12.8	(5.0–20.7)	18.9	(9.6–28.3)	28.8	(18.5–39.2)	21.8	(6.9–36.7)	29.2	(18.9–39.5)	12.0¶	(5.4–18.5)
High school or General Education Development diploma	12.4	(6.6–18.3)	24.2	(17.0–31.5)	20.3	(13.6–26.9)	19.6	(13.7–25.5)	23.5	(17.4–29.6)	17.4	(11.2–23.6)	17.8¶	(12.2–23.4)
Any college or technical school	25.4	(20.4–30.4)	27.8	(23.1–32.5)	27.2	(22.3–32.0)	28.1	(24.0–32.2)	34.9	(30.4–39.5)	34.1	(29.2–39.1)	29.2¶	(25.3–33.1)
Annual household income														
<$25,000	19.4	(14.9–23.9)	23.7	(19.0–28.4)	20.9	(16.7–25.1)	24.6	(20.4–28.8)	26.5	(22.1–31.0)	24.8	(20.2–29.4)	24.4¶	(20.4–28.3)
$25,000–$34,999	35.3	(17.9–52.7)	35.3	(22.8–47.8)	36.6	(24.2–49.0)	31.4	(21.9–40.8)	31.9	(22.0–41.7)	35.3	(23.9–46.7)	29.2¶	(20.1–38.2)
$35,000–$49,999	35.9	(16.7–55.0)	15.4	(4.5–26.3)	25.9	(10.0–41.9)	33.4	(21.3–45.6)	41.1	(27.4–54.8)	35.6	(21.8–49.4)	21.2¶	(12.2–30.2)
≥$50,000	24.2	(8.2–40.2)	35.4	(16.5–54.4)	52.8	(29.6–76.0)	48.3	(34.2–62.4)	48.4	(33.1–63.8)	42.5	(28.9–56.2)	34.6¶	(24.0–45.2)
Total	**20.2¶**	**(16.6–23.8)**	**25.4¶**	**(21.7–29.1)**	**24.2**	**(20.6–27.9)**	**26.2**	**(23.0–29.5)**	**30.9¶**	**(27.3–34.5)**	**29.5**	**(25.8–33.3)**	**24.8¶**	**(21.8–27.8)**

* Daily consumption of a vitamin pill or supplement containing folic acid.
† Denominators varied by characteristic because not all participants responded to all questions.
§ Confidence interval.
¶ Statistically significant ($p<0.05$) difference by chi-square test.

from 22.4% in 1997 to 72.0% in 2003, then decreased to 56.5% in 2006 (Table 2).

In 2006, statistically significant differences in reported knowledge of folic acid and folic acid supplement consumption were observed by age group, education, and household income. Among age groups, a greater percentage of women aged 25–34 years (63.6%) reported knowledge of folic acid than women aged 35–44 years (50.8%). However, a greater percentage of women aged 35–44 years (28.6%) reported folic acid supplement consumption than women aged 18–24 years (20.5%). By education level, a greater percentage of women with any college or technical school education (66.1%) reported knowledge of folic acid than those with high school or General Education Development (GED) diplomas (41.8%) and those with less than a high school education (27.1%). Those with more educa-

TABLE 2. Estimated prevalence of folic acid knowledge* among nonpregnant women aged 18–44 years, by selected characteristics — Behavioral Risk Factor Surveillance System, Puerto Rico, 1997–2006

	1997 (N = 586)		1998 (N = 677)		2000 (N = 996)		2002 (N = 1,091)		2003 (N = 1,034)		2004 (N = 977)		2006 (N = 995)	
Characteristic†	%	(95% CI§)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
Age group (yrs)														
18–24	18.6	(11.6–25.6)	33.6	(25.4–41.8)	61.8	(53.1–70.6)	69.1	(61.9–76.3)	76.2	(69.0–83.5)	62.4	(53.7–71.1)	55.2	(46.9–63.5)
25–34	31.3	(25.0–37.5)	38.9	(32.5–45.2)	57.4	(51.2–63.6)	72.0	(66.3–77.6)	77.1	(71.7–82.6)	70.8	(64.6–77.0)	63.6¶	(57.7–69.5)
35–44	15.3	(10.1–20.5)	32.3	(26.2–38.5)	44.8	(38.8–50.9)	56.2	(51.1–61.4)	64.0	(58.8–69.2)	52.0	(46.7–57.4)	50.8¶	(46.1–55.5)
Education														
Less than high school graduate	6.4	(1.1–11.8)	15.9	(6.8–24.9)	21.6	(12.2–30.9)	41.7	(30.9–52.4)	59.4	(45.5–73.3)	40.7	(29.7–51.7)	27.1¶	(17.7–36.6)
High school or General Education Development diploma	12.7	(7.1–18.4)	24.8	(17.7–31.9)	44.5	(36.4–52.7)	45.1	(37.5–52.7)	63.4	(56.4–70.4)	50.1	(42.3–57.9)	41.8¶	(34.2–49.5)
Any college or technical school	29.7	(24.5–34.8)	42.7	(37.5–47.9)	67.4	(62.7–72.1)	75.7	(71.8–79.7)	76.8	(72.8–80.8)	69.8	(65.0–74.5)	66.1¶	(61.9–70.3)
Annual household income														
<$25,000	20.9	(16.3–25.6)	29.0	(24.2–33.9)	51.8	(46.9–56.8)	60.3	(55.7–64.8)	69.9	(65.5–74.2)	54.5	(49.5–59.6)	52.9¶	(48.3–57.6)
$25,000–$34,999	26.4	(11.5–41.2)	47.1	(34.1–60.0)	63.0	(51.3–74.6)	84.4	(78.1–90.8)	70.6	(60.7–80.6)	72.5	(61.9–83.1)	66.7	(57.1–76.3)
$35,000–$49,999	44.4	(24.9–63.8)	50.4	(34.5–66.3)	63.9	(45.9–81.9)	75.0	(62.9–87.1)	83.2	(73.1–93.3)	81.3	(70.1–92.6)	67.7	(57.2–78.3)
≥$50,000	49.5	(29.4–69.7)	72.5	(53.9–91.0)	63.9	(41.1–86.6)	84.6	(75.0–94.2)	85.4	(76.0–94.7)	81.4	(71.0–91.8)	73.9¶	(63.2–84.5)
Total	**22.4¶**	**(18.7–26.1)**	**35.2¶**	**(31.3–39.2)**	**54.9¶**	**(50.9–59.0)**	**65.4¶**	**(61.9–68.9)**	**72.0¶**	**(68.6–75.4)**	**61.6¶**	**(57.8–65.4)**	**56.5¶**	**(53.0–60.1)**

* Knowing that folic acid is recommended by some health experts for the prevention of birth defects.
† Denominators varied by characteristic because not all participants responded to all questions.
§ Confidence interval.
¶ Statistically significant ($p<0.05$) difference by chi-square test.

tion also were more likely (29.2%) to consume folic acid daily. By income level, women with the highest household incomes (≥$50,000) had a greater percentage of reported knowledge of folic acid (73.9%) and reported folic acid consumption (34.6%) than women with household incomes <$25,000 (52.9% and 24.4%).

Reported by: *L Alvelo-Maldonado, MS; D Valencia Bernal, MS, Puerto Rico Dept of Health. AL Flores, MPH, SD Grosse, PhD, J Mulinare, MD, Div of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, CDC.*

Editorial Note: The end of the decline in NTD (i.e., spina bifida and anencephaly) prevalence in Puerto Rico in recent years is a cause for concern. The decline from 1996 to 2003 likely was aided by a campaign urging women to consume folic acid supplements and by introduction of mandatory folic acid fortification of U.S. cereal grain products in 1998. During a similar period, 1997–2003, reported folic acid supplement consumption and knowledge about folic acid increased among women in Puerto Rico, before declining from 2003 to 2006.

Since 1994, the campaign in Puerto Rico to increase the percentage of women of childbearing age who consume folic acid supplements has resulted in some success. For example, the 24.8% of Puerto Rican women who reported folic acid supplement consumption in 2006 was nearly double the 13.1% prevalence reported by Hispanic women in the mainland United States during 2001–2002 (*6*). However, many women in Puerto Rico associate folic acid use with pregnancy, and their vitamin consumption ends once they are no longer pregnant (*7*). Approximately 66% of pregnancies resulting in live births in Puerto Rico are unintended (*8*); however, even among Puerto Rican women who were aware of folic acid and planned their pregnancies, one study determined that only 54.8% consumed folic acid supplements before pregnancy (*9*).

The findings in this report are subject to at least four limitations. First, because BRFSS survey participants are limited to persons with landline telephones who are not institutionalized, findings might not be representative of the entire population of women aged 18–44 years in Puerto Rico. Second, BRFSS questions relating to folic acid consumption do not specify the recommended daily dose (400 μg) and pertain only to vitamin supplements; therefore, the findings might underestimate or overestimate the actual number of women who consumed the recommended daily dose of folic acid. Third, certain NTD-affected pregnancies might have terminated too early for registration in a hospital, and hospital staff members might not have documented all NTD cases in their log books, resulting in a lower than actual NTD prevalence. Finally, NTDs are rare, and prevalence might be influenced by even slight variations in surveillance methods.

The folic acid campaign in Puerto Rico continues. Campaign staff members attend health fairs throughout the year; and each October on Folic Acid Awareness Day, they distribute educational materials to students at 30 university campuses. In 2006, promotional activities were extended to all public primary and secondary schools. During National Birth Defects Prevention Month in January, articles are placed in newspapers, television interviews are conducted, and partner organizations help to disseminate educational materials. The campaign has developed educational materials on birth defects prevention for health professionals and teachers. However, despite these measures, only approximately one fourth of women of childbearing age in Puerto Rico consume a vitamin containing folic acid daily, suggesting that other factors might affect behavior. Additional measures directed at understanding these factors and promoting folic acid awareness and consumption among all nonpregnant Puerto Rican women of childbearing age are warranted.

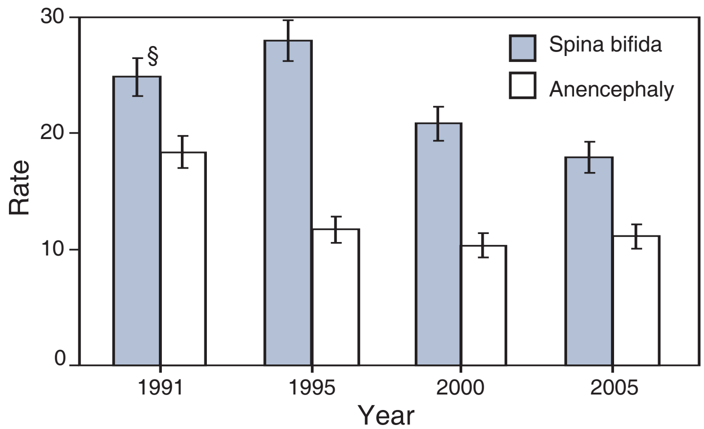
References

1. Mathews TJ, MacDorman MF. Infant mortality statistics from the 2004 period linked birth/infant death data set. Natl Vital Stat Rep 2007; 55(14).
2. Puerto Rico Department of Health, Auxiliary Secretariat for Planning and Development, Division of Statistical Analysis. 2004 annual report. San Juan, Puerto Rico: Puerto Rico Department of Health.
3. Williams LJ, Rasmussen SA, Flores A, Kirby RS, Edmonds LD. Decline in the prevalence of spina bifida and anencephaly by race/ethnicity: 1995–2002. Pediatrics 2005;116:580–6.
4. Puerto Rico Department of Health, Auxiliary Secretariat of Family Health and Integrated Services, Mother and Child Health Care Division, Puerto Rico Birth Defects Surveillance System. 2007 annual report. San Juan, Puerto Rico: Puerto Rico Department of Health.
5. Williams LJ, Mai CT, Edmonds LD, et al. Prevalence of spina bifida and anencephaly during the transition to mandatory folic acid fortification in the United States. Teratology 2002;66:33–9.
6. Yang QH, Carter HK, Mulinare J, Berry RJ, Friedman JM, Erickson JD. Race-ethnicity differences in folic acid intake in women of childbearing age in the United States after folic acid fortification: findings from the National Health and Nutrition Examination Survey, 2001–2002. Am J Clin Nutr 2007;85:1409–16.
7. Lindsey LLM, Hamner HC, Prue CE, et al. Understanding optimal nutrition among women of childbearing age in the United States and Puerto Rico: employing formative research to lay the foundation for National Birth Defects Prevention Campaigns. J Health Comm 2007;12:733–57.
8. Puerto Rico Department of Health, Auxiliary Secretariat of Family Health and Integrated Services, Mother and Child Health Care Division, Monitoring and Evaluation Section. Puerto Rico Maternal-Infant Health Survey, 2006. San Juan, Puerto Rico: Puerto Rico Department of Health.
9. De la Vega A, Salicrup E, Verdiales M. A nationwide program for the use of preconceptional folic acid to prevent the development of open neural tube defects. Who is really using folic acid? P R Health Sci J 2002;21:7–9.

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Spina Bifida and Anencephaly Rates* — United States, 1991, 1995, 2000, and 2005†



* Per 100,000 live births. Annual data on birth defects are based on information reported on birth certificates provided through the National Vital Statistics System. Because of challenges associated with the reporting of birth defects during the period immediately after birth, spina bifida and anencephaly are considered underreported on birth certificates. Additional information is available at http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_06.pdf.

† Excludes data from Maryland, New Mexico, and New York, which did not require reporting for certain years.

§ 95% confidence interval.

Neural tube defects (NTDs) are serious birth defects of the brain (anencephaly) and spine (spina bifida). Since 1992, a national health recommendation has called for women of childbearing age in the United States to consume 400 μg of folic acid daily to reduce their risk for having a pregnancy affected by NTDs. The spina bifida rate per 100,000 live births declined 25% from 1995 to 2000 and 13% from 2000 to 2005. The anencephaly rate declined 36% from 1991 to 1995 and was unchanged from 1995 to 2005.

SOURCE: Mathews TJ. Trends in spina bifida and anencephalus in the United States, 1991–2005. National Vital Statistics System. Available at http://www.cdc.gov/nchs/products/pubs/pubd/hestats/spine_anen.htm.