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Reproductive Hazards

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Men, women, and children who live or work on farms around the world are exposed to many different types of potentially harmful agents that can interfere with reproductive development and function. Exposures to physical, chemical and biological hazards can occur during normal farm work from handling animals or their bodily fluids, working with chemicals or working in areas where chemicals have been used, and operating farm equipment.

Fertility, gestation, and pregnancy outcome are dependent on complex biological processes beginning early in life. Disruption of these processes can happen with environmental exposures *in utero* and throughout childhood development, as well as in adulthood through occupational and environmental exposures. Interference with development or functioning of the reproductive tract in males and females can result in diminished fertility, infertility, adverse pregnancy outcomes, congenital malformations, and childhood cancer.

Studies have documented associations between living or working in an agricultural area and adverse reproductive outcomes. Exposure to chemicals, mainly pesticides, has been linked to infertility and diminished fertility, spontaneous abortion, birth defects, and childhood cancer. A large number of studies suggest pesticide exposure is associated with these adverse reproductive outcomes, but few studies quantify the type of pesticide or measure exposure levels. Biomarkers of pesticides exposure have been measured in both male and female reproductive tracts, breast milk, and semen. Pesticides have also been measured in amniotic fluid, meconium, and cord blood, indicating the fetus is exposed to pesticides throughout development. These measurements provide some evidence to strengthen the association between pesticide exposure and reproductive outcomes but do not prove causality (1–6).

It is plausible that pesticides in semen may have direct effects on sperm or can be transmitted to the woman and fetus. Likewise, pesticides in the female reproductive tract could interfere with oocyte development, ovulation, fertilization, implantation, pregnancy, and development of the fetus. However,

there are no studies to date linking these biological measurements with adverse reproductive outcomes (1–6).

The term *pesticides* includes a wide variety of chemicals (see Chapters 13 and 16). In addition, many pesticide formulations contain solvents that have also been associated with reproductive toxicity. Adverse reproductive outcomes including decreased sperm count, infertility, testicular cancer, cryptorchidism, and hypospadias have been linked to widespread use of chemicals with hormonal properties, the so-called endocrine disruptors. A number of pesticides, especially organochlorines, have been identified as endocrine disruptors. In developing countries, workers are exposed to increasing amounts of pesticides, including some banned in prosperous countries. Prevention should include decreased total exposure by the elimination or reduction of chemicals, integrated pest management, proper personal protective equipment, and improved work practices (7–10).

Chemical Reproductive Hazards

Infertility in Males

Occupational and environmental chemical exposures in an agricultural environment have been associated with infertility in men. A number of pesticides have been associated with poor semen quality, including dibromochloropropane (DBCP), ethylene dibromide, carbaryl, chlordecone (Kepone), and 2, 4-D. The use of many of these pesticides has been banned or severely restricted (11–15).

There are a number of studies linking poor semen quality with pesticide exposure. In one well-designed study of environmental pesticide exposure, urine metabolites of pesticides were correlated to semen quality in known fertile men. Decreased semen quality was associated with exposure to the herbicides atrazine and alachlor and the insecticide diazinon. A study of men seeking infertility treatment in Argentina found pesticide exposure was associated with lower sperm counts and poor semen quality, although specific pesticides were not identified or measured. In a study of patients undergoing in vitro fertilization, high paternal pesticide exposure was associated with decreased fertilization rates. A study in Mexico demonstrated urinary metabolites of organophosphates were associated with an increased frequency of sperm sex-null aneuploidy and alterations in sperm chromatin structure. While there are no studies of semen pesticide levels and reproductive outcomes, it is plausible that poor semen quality could result in infertility or an increased time-to-pregnancy. Sperm chromosomal abnormalities could result in infertility, spontaneous abortion or birth defects (11,13,16,17,18).

High levels of pesticide exposures in pesticide applicators and greenhouse workers have been associated with increased time-to-pregnancy. The use of

pyrethoids has been similarly associated. However, a large multicenter study found no difference in time-to-pregnancy between traditional and organic farmers. Other studies have found no differences between time-to-pregnancy in greenhouse workers who use personal protective equipment compared to unexposed workers. Differences in working conditions, types of pesticides used, and levels of exposure may account for the discrepancis in these studies (19–22).

Infertility in Females

Although there are some reported associations between female infertility and agricultural work, there are no studies using direct exposure data to assess outcomes. Biomarker studies have measured pesticide residues in the female reproductive tract, indicating exposures and uptake are occurring in critical tissues, but there are no studies to date linking these measurements with infertility. High levels of p,p′-DDE, a metabolite of the pesticide DDT, were found in sera and follicular fluid samples of women attending an infertility program and were associated with poor fertilization rates (1).

There are a number of small studies where associations between working with pesticides and infertility or increased time-to-pregnancy were found. Fuortes found women were at an increased risk of infertility if they had worked in the agricultural industry or resided on a farm. In the same study, the risk of being diagnosed with an ovulatory or tubal cause of infertility was increased 4- to 16-fold among those working in agriculture (23–25).

Pregnancy Outcomes

Spontaneous abortion, defined as termination of pregnancy before 20 weeks gestation, has been associated with both maternal and paternal pesticide exposures. However, most studies have small numbers of subjects and do not classify or quantify pesticide exposure. A 3-fold increase in spontaneous abortions was found for paternal exposure to DBCP. A preliminary study of Chinese women found a weak association between serum DDE levels and increased incidence of spontaneous abortion. Studies in Ontario have suggested an increase in spontaneous abortions with paternal use of dithiocarbamates and carbaryl. A retrospective cohort study of farming households in the Phillipines found an increased risk of spontaneous abortion with increased pesticide use. A moderate increase in spontaneous abortion was observed in both female workers and the wives of male workers in the floriculture industry in Colombia. Other studies have found no association (26–31).

There are limited studies of the pregnancy outcomes of pre-term labor, small-for-gestational age, or low birth weight babies. The Ontario Farm Family Health Study found a weak association for mixing or applying herbicides and pre-term labor. However, other studies have not found any association

between parental pesticide exposure and pre-term labor. A recent study measuring maternal urinary and cord blood organophosphates and cholinesterase levels found a small decrease in gestational age but no association with intrauterine growth retardation (IUGR). A preliminary study found IUGR was associated with elevated levels of atrazine and other herbicides in drinking water in rural Iowa. A small but significant decrease in birth weight was associated with maternal pyrethoid use. Other studies have found no association with agricultural occupations and low birthweight (28–33).

Birth Defects

There are conflicting studies of the associations of agricultural work and pesticide exposure with birth defects. As in most studies examining reproductive outcomes and pesticide exposure, incomplete data are available on the types of pesticides associated with these defects and biomarkers of exposure. One large study of the Norway birth registry from 1967 to 1991 found activities involving high pesticide exposure and conception during times of high pesticide use (April to June) were associated with an increased risk of central nervous system defects, neural tube defects, limb reductions, and the genitourinary birth defects of hypospadias and cryptorchidism. Some studies have supported these findings while others have found risk estimates close to unity. Other studies have found an association with oral clefts and agriculture work. One difficulty in these studies is that the number of birth defects reported is very small and must be pooled for statistical power. Most of the studies on the risk of birth defects for paternal occupational exposures to pesticides do not find any associations or only small increased risks (31,34–40).

In Spain, maternal pesticide exposure during the first trimester was associated with an increased risk of central nervous system defects and oral clefts. Conventional pesticide use in the Phillipines was associated with increased risk of birth defects compared to low pesticide use (29,41).

Childhood Cancer

Although there is no strongly consistent evidence, a number of studies have found associations between childhood cancer and parental agricultural occupations or exposures. A large international study found associations between childhood brain tumors and various farm-related activities including maternal exposure to farm animals, working on a farm and pesticide exposure. In the same study, maternal exposure to pigs was associated with a 4-fold increase in risk of primitive neuroectodermal tumors. Other studies have found similar results. Chemicals, such as those found in a farm environment, and microbes that could be found in farm animals have been hypothesized to

cause childhood brain tumors. However, there is no direct evidence for this association (42–44).

Occupational parental pesticide use is associated with leukemia, childhood brain cancer, Wilm's tumor, and Ewing's sarcoma. Use of pesticides in gardens has been associated with childhood leukemia in Northern Germany and other countries. Other studies have found no association with paternal exposures to pesticides and childhood cancer. A large study of males born to parents engaged in agricultural activity between 1952 to 1991 in Norway found specific fertilizers were associated with an increased rate of testicular cancer, in particular, seminoma. Renal cancer has been associated with paternal exposure to pesticides in one small study (45–50).

Biologic Reproductive Hazards

A variety of organisms found in the agricultural setting have been associated with adverse reproductive outcomes, including miscarriage, stillbirth, congenital infections, and birth defects. These organisms include viruses, bacteria, and parasites associated with farm animals or working outdoors (51).

Toxoplasmosis

Toxoplasmosis gondii is passed to humans through contact with infected animal feces, usually cats, or ingestion of contaminated meat. Direct contact with cats does not usually result in infection; however, stray cats or cats roaming on farms may contaminate the environment with *T. gondii oocysts*. In 1977, an outbreak of acute toxoplasmosis occurred in a riding stable in Atlanta that was linked to inhalation of aerosolized oocysts shed by cats in the stable. A multicenter case-control study in Europe found contact with soil was a strong risk factor for toxoplasmosis infection, attributed to 6% to 17% of primary infections in humans.

Infections during pregnancy are transplacentally transmitted to the fetus and can cause fetal death or permanent neurological damage. In the United States, sero-positivity is about 15%, but in some African countries the prevalence approaches 80%. Reports of stillbirth caused by toxoplasmosis in developed countries are rare. However, in developing countries where the prevalence may be much higher the contribution is unknown. Pregnant women should avoid contact with cat feces and wear gloves when working in soil (51).

Q Fever

This rickettsial infection is caused by the bacteria *Coxiella burnetti* and is transmitted to humans during contact with infected parturient products, tick bites, and ingestion of infected dairy products. Cattle, sheep, and goats are

considered the primary reservoirs from which human infections occur. Human infections have been described worldwide and infections during pregnancy have been associated with abortion, stillbirth, low birthweight, and preterm labor. Atypical pneumonia and hepatitis are common presentations. A review of reported cases found two-thirds of untreated cases during the first trimester resulted in fetal death, while infection during the second trimester was associated with pre-term labor. Primary infection during the first 6 months of pregnancy is also associated with chronic infection. Long-term co-trimoxazole treatment can prevent fetal death but not the development of chronic infection. The overall contribution of Q Fever to poor pregnancy outcomes is unknown. Other rickettsial infections, such as Rocky Mounted Spotted Fever, have not been associated with poor pregnancy outcomes (51–54).

Psittacosis

A flu-like systemic infection caused by *Chlamydia psittaci*. Most cases of psittacosis result from inhaling infectious material from diseased birds. Infection can also result from contact with infected birth fluids and membranes of goats and sheep. Although human infection is rare, infections in pregnant women have been reported after exposure to birth fluids of otherwise healthy-appearing infected sheep and goats or through contact with birds. The majority of these cases resulted in fetal death due to spontaneous abortion or premature delivery (55–56).

Maternal infection can be severe, but full recovery usually occurs once the infant is delivered, although maternal death has been reported. Favorable outcomes can be achieved with prompt diagnosis and treatment, including emergency delivery of the infant when appropriate. Neonates are not always infected. Prevention includes avoidance of contact with membranes or birth fluids of sheep and goats or contact with birds during pregnancy. Strict personal hygiene should be practiced as the primary route of infection is oropharyngeal (56).

Brucellosis

This is caused by various species of the *Brucella* bacterium. Brucellosis is found worldwide and is transmitted to humans through direct contact with infected animals. Major reservoirs include goats and sheep (*B. melitensis*), swine (*B. suis*), cattle (*B. abortus*), and dogs (*B. canis*). Outcomes associated with infection during pregnancy are not well known and transmission to the fetus is speculated to occur through the placenta. Whether infection leads to fetal death is controversial. Manifestations of neonatal brucellosis include

low birth weight, fever, failure to thrive, jaundice, and hepatosplenomegaly. Antibiotic treatment during pregnancy may prevent abortion and premature delivery (57).

Leptospirosis

The causative organism, *Leptospira interrogans*, is a spirochete commonly found in Latin America. It is excreted in urine of infected animals and enters humans through non-intact skin, mucous membranes, and by inhalation and ingestion. It is usually a self-limiting disease, and, although rare in pregnancy, the organism has been detected in the placenta and amniotic fluid. Infections have been associated with fetal death in up to 50% of cases as well as active disease in newborn infants. Early diagnosis with urine and serological tests and treatment with antibiotics is critical (58).

Swine Influenza

This viral infection is thought to have been responsible for the worldwide pandemic that caused an estimated 40 million deaths in 1918 to 1919. During this epidemic, pregnancy was associated with a high mortality rate of over 50% if pneumonia was present. Since this pandemic, reports of swine influenza cases have been rare, with only sporadic case reports of human illness in the United States, Europe, and Russia. There is a case report of a previously healthy pregnant woman who acquired swine influenza while visiting a swine barn at a county fair. The swine were reported to exhibit influenza-like symptoms. The infection resulted in maternal respiratory failure and death, but the infant survived and was asymptomatic. There is no increase in influenza morbidity and mortality among pregnant women during non-pandemic years. Based on the few case reports and historical information from the swine flu pandemic of 1918, pregnant women are advised to avoid contact with swine that exhibit signs of respiratory illness (59).

Malaria

Infections during pregnancy result in a range of adverse pregnancy outcomes, especially pre-term delivery and IUGR. More than 40% of all births worldwide occur in areas with endemic malaria. Pregnant women experiencing a malaria infection for the first time are at high risk for stillbirth. Prevention is based primarily on environmental control, avoidance of mosquitoes, use of repellents, and bed netting. Repellents with DEET are considered safe for pregnant women (51).

West Nile Virus

West Nile Virus (WNV) is transmitted by infected mosquitoes. The reservoir exists in migratory birds and horses. Based on a limited number of cases, it is not possible to know if WNV infection in pregnancy results in neonatal infection or medical problems. Although one of the first reported cases of WNV infection transmitted via the placenta resulted in an infected infant with severe medical problems, it is unclear whether WNV infection caused these problems or whether they were due to other causes. A registry has been set up by the U.S. Centers for Disease Control to monitor cases of WNV infection in pregnant women. As of May 10, 2004, of the 74 women who acquired WNV while pregnant, 62 had delivered live infants, 2 had elective abortions, 5 miscarried in the first trimester, and 5 had not yet delivered. Because of ongoing concerns that intrauterine transmission can occur with possible adverse health effects, pregnant women are advised to take precautions to reduce their risk of infection by avoiding mosquitoes, especially during peak feeding times of dawn and dusk, wearing protective clothing, and using repellents. No specific treatment exists for WNV, and the consequences during pregnancy have not been well defined. Accordingly, it is not recommended that asymptomatic women be screened (60).

Lyme Disease

Caused by the tick-borne spirochete, *Borrelia burgdorferi*, Lyme disease is found in North America, Europe, Australia, China, Japan, and Africa. People who live or work in residential areas surrounded by tick-infested woods or overgrown brush are at risk. Lyme disease is a systemic illness that has been associated with stillbirth. The first cases were described in the mid-1980s, and the organism has been found in fetal organs. However, a large serological series found few adverse reproductive outcomes associated with Lyme disease. Preventive measures and early recognition of the disease are important. Early treatment with antibiotics decreases the morbidity from Lyme disease. In endemic areas, Lyme disease can be diagnosed if the typical "target" skin lesion is present even if serological tests are negative. Pregnant women should be treated with penicillin (51).

Physical Reproductive Hazards

Physical hazards in an agricultural setting that can impact reproductive outcomes are primarily associated with activities during pregnancy. Few studies have looked specifically at physical hazards in an agricultural occupation. A number of studies have associated poor pregnancy outcomes with activities

that are common in agricultural work: physical labor, heavy lifting, long hours, and shift work.

Jobs that involve an increase in abdominal pressure (bending and lifting), standing 6 or more hours per day, working more than 40 hours per week, and performing heavy lifting have been consistently associated with an increased incidence of spontaneous abortion and pre-term delivery. Shift work has also been associated with pre-term delivery. Outcomes of low birth-weight have not been as consistently associated with physically strenuous work. One study found long weeks of physically demanding work could result in a decrease in fetal weight, but no association was found for pre-term delivery. Occupational noise exposure at levels of 85 dB has been inconsistently associated with low birth-weight. Heat stress can also contribute to adverse fetal outcomes in the last trimester of pregnancy (32,61–64).

Whenever possible, heavy work duties should be modified and frequent rest periods taken throughout pregnancy to lower the risk of adverse pregnancy outcomes. If not possible, then more frequent clinician visits and placement in pre-term birth prevention classes may be valuable.

Conclusion

There is ample evidence that agricultural workers and those who reside in agricultural areas have an increased risk for a variety of adverse reproductive health outcomes. Both paternal and maternal exposures to biologic and chemical agents and maternal exposure to physical factors must be recognized and controlled to prevent these adverse effects on fertility and on the next generation of children. Strategies should include reduction or elimination of chemical agents whenever possible, proper personal protective equipment, improved work practices and hygiene, worker education, avoidance of biologic exposures, and reduction in the intensity and duration of maternal physical labor.

References

1. Younglai EV, Foster WG, Hughes EG, Trim K, Jarrell JF. Levels of environmental contaminants in human follicular fluid, serum, and seminal plasma of couples undergoing in vitro fertilization. Arch Environ Contam Toxicol 2202;43:121–26.
2. Arbuckle TE, Schrader SM, Cole D, Hall JC, Bancej CM, Turner LA, Claman P. 2,4-Dichlorophenoxyacetic acid residues in semen of Ontario farmers. Reprod Toxicol 1999;13:421–29.
3. Kunisue T, Someya M, Monirith I, Watanabe M, Tana TS, Tanabe S. Occurrence of PCBs, organochlorine insecticides, tris(4-Chlorophenyl)methane, and tris(4-chlorophenyl)methanol in human breast milk collected from Cambodia. Arch Environ Contam Toxicol 2004;46:405–12.

4. Anwar WA. Biomarkers of Human Exposure to Pesticides. Environ Health Perspect 1997;105:801–6.
5. Solomon GM, Weiss PM. Chemical contaminants in breast milk: Time trends and regional variability. Environ Health Perspect 2002;110:A339–47.
6. Bradman A, Barr DB, Henn BGC, Drumheller T, Curry C, Eskenazi B. Measurement of pesticides and other toxicants in amniotic fluid as a potential biomarker of prenatal exposure: a validation study. Environ Health Perspect 2003;111:1779–82.
7. Foster W, Chan S, Platt L, Hughes C. Detection of endocrine disrupting chemicals in samples of second trimester human amniotic fluid. J Clin Endocrinol Metab. 2000;85:2954–57.
8. Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Declining semen quality and increasing incidence of testicular cancer: is there a common cause? Environ Health Perspect 1995;103(Suppl7):137–9.
9. Colborn T, vom Saal FS, Soto AM. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. Environ Health Perspect 1993;101: 378–84.
10. Sharpe RM, Skakkebaek NE. Are oestrogens involved in falling sperm counts and disorders of the male reproductive tract? Lancet 1993;341:1392–5.
11. Oliva A, Spira A, Multigner L. Contribution of environmental factors to the risk of male infertility. Hum Reprod 2001;16:1768–76.
12. Strohmer H, Boldizsar A, Plockinger B, Feldner-Busztin M, Feichtinger W. Agricultural work and male infertility. Am J Ind Med 1993;24:587–92.
13. Swan SH, Kruse RL, Liu F, Barr DB, Drobnis EZ, Redmon JB, Wang C, Brazil C, Overstreet JW. Semen quality in relation to biomarkers of pesticide exposure. Environ Health Perspect 2003;111:1478–84.
14. Larsen SB, Joffe M, Bonde JP. Time-to-pregnancy and exposure to pesticides in Danish farmers. ASCLEPIOS Study Group. Occup Environ Med 1998;55:278–83.
15. Lerda D, Rizzi R. Study of reproductive function in persons occupationally exposed to 2,4-dichlorophenoxyacetic acid (2,4-D). Mutation Research 1991; 262:47–50.
16. Tielemans E, van Kooij R, te Velde E, Burdorf A, Heederik D. Pesticide exposure and decreased fertilization rates in vitro. The Lancet 1999;354:484–85.
17. Recio R, Robbins WA, Borja-Aburto V, Moran-Martinez J, Froines JR, Hernandez RM, Cebrian ME. Organophosphorous pesticide exposure increases the frequency of sperm sex-null aneuploidy. Environ Health Perspect 2001;109: 1237–40.
18. Sanchez-Pena LC, Reyes BE, Lopez-Carrillo L, Recio R, Moran-Martinez J, Cebrian ME, Quintanilla-Vega B. Organophosphorous pesticide exposure alters sperm chromatin structure in Mexican agricultural workers. Toxicol Appl Pharm 2004;196:108–13.
19. de Cock J, Westveer K, Heederik D, te Velde E, van Kooij R. Time-to-pregnancy and occupational exposure to pesticides in fruit growers in The Netherlands. Occup Environ Med 1994;51:693–99.
20. Petrelli G, Figa-Talamanca I. Reduction in fertility in male greenhouse workers exposed to pesticides. Eur J Epidemiol 2001;17:675–7.
21. Sallmen M, Liesivuori J, Taskinen H, Lindbohm ML, Anttila A, Aalto L, Hemminki K. Time-to-pregnancy among the wives of Finnish greenhouse workers. Scand J Work Environ Health 2003;29:85–93.

22. Thonneau P, Abell A, Larsen SB, Bonde JP, Joffe M, Clavert A, Ducot B, Multigner L, Danscher G. Effects of pesticides on time-to-pregnancy. Am J Epidemiol 1999;150:157–63.
23. Abell A, Juul S, Bonde JP. Time-to-pregnancy among female greenhouse workers. Scand J Work Environ Health 2000;26:131–6.
24. Greenlee AR, Arbuckle TE, Chyou PH. Risk factors for female infertility in an agricultural region. Epidemiology 2003;14:429–36.
25. Fuortes L, Clark MK, Kirchner HL, Smith EM. Association between female infertility and agricultural work history. Am J Ind Med 1997;31:445–51.
26. Goldsmith JR. Dibromochloropropane: epidemiological findings and current questions. Ann N Y Acad Sci 1997;837:300–6.
27. Korrick SA, Chen C, Damokosh AI, Ni J, Liu X, Cho SI, Altshul L, Ryan L, Xu X. Association of DDT with spontaneous abortion: a case-control study. Ann Epidemiol 2001;11:491–6.
28. Savitz DA, Arbuckle T, Kaczor D, Curtis KM. Male pesticide exposure and pregnancy outcome. Am J Epidemiol 1997;146:1025–36.
29. Crisostomo L, Molina VV. Pregnancy outcomes among farming households of Nueva Ecija with conventional pesticide use versus integrated pest management. Int J Occup Environ Health 2002;8:232–42.
30. Restrepo M, Munoz N, Day NE, Parra JE, de Romero L, Nguyen-Dinh X. Prevalence of adverse reproductive outcomes in a population occupationally exposed to pesticides in Colombia. Scand J Work Environ Health 1990;16: 232–38.
31. Nurminen T. Maternal pesticide exposure and pregnancy outcome. J Occup Environ Med 1995;37:935–40.
32. Gold EB, Tomich E. Occupational hazards to fertility and pregnancy outcome. In: Gold EB, Lasley BL, Schenker MB (eds.), Occupational Medicine, State of the Art Reviews. Reproductive Hazards 1994;9:435–69.
33. Eskenazi B, Harley K, Bradman A, Weltzien E, Jewell NP, Barr DB, Furlong CE, Holland NT. Association of *in utero* organophosphate pesticide exposure and fetal growth and length of gestaion in an agricultural population. Environ Health Perspect 2004;112:1116–24.
34. Munger R, Isacson P, Hu S, Burns T, Hanson J, Lynch CF, Cherryholmes K, Van Dorpe P, Hausler W. Intrauterine growth retardation in Iowa communities with herbicide-contaminated drinking water supplies. Environ Health Perspect 1997;105:308–14.
35. Kristensen P, Irgens LM, Andersen A, Bye AS, Sundheim L. Birth defects among offspring of Norwegian farmers, 1967–1991. Epidemiology 1997;8:537–44.
36. Engel LS, O'Meara ES, Schwartz SM. Maternal occupation in agriculture and risk of limb defects in Washington State, 1980–1993. Scand J Work Environ Health 2000;26:193–8.
37. Blatter BM, Roeleveld N, Bermejo E, Martinez-Frias ML, Siffel C, Czeizel AE. Spina bifida and parental occupation: results from three malformation monitoring programs in Europe. Eur J Epidemiol 2000;16:343–51.
38. Garcia AM. Occupational exposure to pesticides and congenital malformations: a review of mechanisms, methods, and results. Am J Ind Med 1998;33:232–40.
39. Nurminen T, Rantala K, Kurppa K, Holmberg PC. Agricultural work during pregnancy and selected structural malformations in Finland. Epidemiology 1995;6:23–30.

40. Garcia AM, Benavides FG, Fletcher T, Orts E. Paternal exposure to pesticides and congenital malformations. Scand J Work Environ Health 1998;24:473–80.
41. Garcia AM, Fletcher T, Benavides FG, Orts E. Parental agricultural work and selected congenital malformations. Am J Epidemiol 1999;149:64–74.
42. Efird JT, Holly EA, Preston-Martin S, Mueller BA, Lubin F, Filippini G, Peris-Bonet R, McCredie M, Cordier S, Arslan A, Bracci PM. Farm-related exposures and childhood brain tumours in seven countries: results from the SEARCH International Brain Tumour Study. Paediatr Perinat Epidemiol 2003;17:201–11.
43. Holly EA, Bracci PM, Mueller BA, Preston-Martin S. Farm and animal exposures and pediatric brain tumors: results from the United States West Coast Childhood Brain Tumor Study. Cancer Epidemiol Biomarkers Prev 1998;7: 797–802.
44. Kristensen P, Andersen A, Irgens LM, Bye AS, Sundheim L. Cancer in offspring of parents engaged in agricultural activities in Norway: incidence and risk factors in the farm environment. Int J Cancer 1996;65:39–50.
45. Zahm SH, Ward MH. Pesticides and childhood cancer. Environ Health Perspect 1998;106:893–908.
46. Daniels JL, Olshan AF, Savitz DA. Pesticides and childhood cancers. Environ Health Perspect 1997;105:1068–77.
47. Meinert R, Kaatsch P, Kaletsch U, Krummenauer F, Miesner A, Michaelis J. Childhood leukaemia and exposure to pesticides: results of a case-control study in northern Germany. Eur J Cancer 1996;32A:1943.
48. Rodvall Y, Dich J, Wiklund K. Cancer risk in offspring of male pesticide applicators in agriculture in Sweden. Occup Environ Med 2003;60:798–801.
49. Kristensen P, Andersen A, Irgens LM, Bye AS, Vagstad N. Testicular cancer and parental use of fertilizers in agriculture. Cancer Epidemiol Biomarkers Prev 1996;5:3–9.
50. Fear NT, Roman E, Reeves G, Pannett B. Childhood cancer and paternal employment in agriculture: the role of pesticides. Br J Cancer 1998;77:825–9.
51. Goldenberg RL, Thompson C. The infectious origins of stillbirth. Am J Obstet Gynecol 2003;189:861–73.
52. Tenter AM, Heckeroth AR, Weiss LM. Toxoplasma gondii: from animals to humans. Int J Parasitol 2000;30:1217–58.
53. Maurin M, Raoult D. Q fever. Clin Microbiol Rev 1999;12:518–53.
54. Raoult D, Fenollar F, Stein A. Q fever during pregnancy: diagnosis, treatment, and follow-up. Arch Intern Med 2002;162:701–4.
55. Jorgensen DM. Gestational psittacosis in a Montana sheep rancher. Emerg Infect Dis 1997;3:191–4.
56. Flanagan PG, Westmoreland D, Stallard N, Stokes IM, Evans J. Ovine Chlamydiosis in pregnancy. Br J Obstet Gynaecol 1996;103:382–5.
57. Giannacopoulos I, Eliopoulou MI, Ziambaras T, Papanastasiou DA. Transplacentally transmitted congenital brucellosis due to *Brucella abortus*. J Infect 2002;45:209–10.
58. Chedraui PA, San Miguel G. A case of leptospirosis and pregnancy. Arch Gynecol Obstet 2003;269:53–4.
59. McKinney WP, Volkert P, Kaufman J. Fatal swine influenza pneumonia during late pregnancy. Arch Intern Med 1990;150:213–5.
60. Interim guidelines for the evaluation of infants born to mothers infected with West Nile virus during pregnancy. MMWR Morb Mortal Wkly Rep 2004; 53:154–7.

61. Paul M. Occupational and Environmental Reproductive Hazards. Baltimore: Williams and Wilkins,1993.
62. Nurminen T. Female noise exposure, shift work, and reproduction. J Occup Environ Med 1995;37:945–50.
63. Hatch M, Ji BT, Shu XO, Susser M. Do standing, lifting, climbing, or long hours of work during pregnancy have an effect on fetal growth? Epidemiology 1997;8:530–6.
64. Engberg L. Women and Agricultural Work. Occupational Medicine. State of the Art Reviews 1993;8:869–82.

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