Article 5

THE MYSTERY OF FETAL LIFE:
SECRETS OF THE WOMB

JOHN PEKKANEN

In the dim light of an ultrasound room, a wand slides over the abdomen of a young woman. As it emits sound waves, it allows us to see into her womb. The video screen brightens with a grainy image of a 20-week-old fetus. It floats in its amniotic sac, like an astronaut free of gravity.

The fetal face stares upward, then turns toward us, as if to mug for the camera. The sound waves strike different tissues with different densities, and their echoes form different images. These images are computer-enhanced, so although the fetus weights only 14 ounces and is no longer than my hand, we can see its elfin features.

Close up, we peek into the fetal brain. In the seconds we observe, a quarter million new brain cells are born. This happens constantly. By the end of the nine months, the baby's brain will hold 100 billion brain cells.

The sound waves focus on the chest, rendering images of a vibrating four-chambered heart no bigger than the tip of my little finger. The monitor tells us it is moving at 163 beats a minute. It sounds like a frightened bird fluttering in its cage.

We watch the rib cage move. Although the fetus lives in an airless environment, it "breathes" intermittently inside the womb by swallowing amniotic fluid. Some researchers speculate that the fetus is exercising its chest and diaphragm as its way of preparing for life outside the womb.

The clarity of ultrasound pictures is now so good that subtle abnormalities can be detected. The shape of the skull, brain, and spinal cord, along with the heart and other vital organs, can be seen in breathtaking detail.

In this ultrasound exam, there are no hints to suggest that anything is abnormal. The husband squeezes his wife's hand. They both smile.

The fetus we have just watched is at the midpoint of its 40-week gestation. At conception 20 weeks earlier, it began as a single cell that carried in its nucleus the genetic code for the human it will become.

After dividing and redividing for a week, it grew to 32 cells. Like the initial cell, these offspring cells carry 40,000 or so genes, located on 23 pairs of chromosomes inherited from the mother and father. Smaller than the head of a pin, this clump of cells began a slow journey down the fallopian tube and attached itself to the spongy wall of the uterus.

Once settled, some embryonic cells began to form a placenta to supply the embryo with food, water, and nutrients from the mother's bloodstream. The placenta also filtered out harmful substances in the mother's bloodstream. The embryo and mother exchange chemical information to ensure that they work together toward their common goal.

Instructed by their genes, the cells continued to divide but didn't always produce exact replicas. In a process still not well understood, the cells began to differentiate to seek out their own destinies. Some helped build internal organs, others bones, muscles, and brain.

At 19 days postconception, the earliest brain tissues began to form. They developed at the top end of the neural tube, a sheath of cells that ran nearly the entire length of the embryo.

The human brain requires virtually the entire pregnancy to emerge fully, longer than the other organ systems. Even in the earliest stage of development, the fetus knows to protect its brain. The brain gets the most highly oxygenated blood, and should there be any shortage, the fetus will send the available blood to the brain.

Extending downward from the brain, the neural tube began to form the spinal cord. At four weeks, a rudimentary heart started to beat, and four limbs began sprouting. By eight weeks, the two-inch-long embryo took human form and was more properly called a fetus. At 10 to 12 weeks, it began moving its

arms and legs, opened its jaws, swallowed, and yawned, Mostly it slept.

"We are never more clever than we are as a fetus," says Dr. Peter Nathanielsz, a fetal researcher, obstetrician, and professor of reproductive medicine at Cornell University. "We pass far more biological milestones before we are born than we'll ever pass after we're born."

Not long ago, the process of fetal development was shrouded in mystery. But through the power of scanning techniques, biotechnology, and fetal and animal studies, much of the mystery of fetal life has been unveiled.

We now know that as the fetus matures it experiences a broad range of sensory stimulation. It hears, sees, tastes, smells, feels, and has rapid eye movement (REM) sleep, the sleep stage we associate with dreaming. From observation of its sleep and wake cycles, the fetus appears to know night from day. It learns and remembers, and it may cry. It seems to do everything in utero that it will do after it is born. In the words of one researcher, "Fetal life is us."

Studies now show that it's the fetus, not the mother, who sends the hormonal signals that determine when a baby will be born. And we've found out that its health in the womb depends in part on its mother's health when she was in the womb.

Finally, we've discovered that the prenatal environment is not as benign, or as neutral, as once thought. It is sensitive to the mother's health, emotions, and behavior.

The fetus is strongly affected by the mother's eating habits. If the mother exercises more than usual, the fetus may become temporarily short of oxygen. If she takes a hot bath, the fetus feels the heat. If she smokes, so does the fetus. One study has found that pregnant women exposed to more sunlight had more-outgoing children.

We now know that our genes do not encode a complete design for us, that our "genetic destiny" is not hard-wired at the time of conception. Instead, our development involves an interplay between genes and the environment, including that of the uterus. Because genes take "cues" from their environment, an expectant mother's physical and psychological health influences her unborn child's genetic well-being.

Factors such as low prenatal oxygen levels, stress, infections, and poor maternal nutrition may determine whether certain genes are switched on or off. Some researchers believe that our time in the womb is the single most important period of our life.

"Because of genetics, we once thought that we would unfold in the womb like a blueprint, but now we know it's not that simple," says Janet DiPietro, an associate professor of maternal and child health at the Johns Hopkins School of Public Health and one of a handful of fetal-behavior specialists. "The mother and the uterine environment she creates have a major impact on many aspects of fetal development, and a number of things laid down during that time remain with you throughout your life."

The impact of the womb on our intelligence, personality, and emotional and physical health is beginning to be understood. There's also an emerging understanding of something called fetal programming, which says that the effects of our life in the womb may be not felt until decades after we're born, and in ways that are more powerful than previously imagined.

Says Dr. Nathanielsz, whose book *Life in the Womb* details the emerging science of fetal development: "It's an area of great scientific importance that until recently remained largely unknown."

"I'm pregnant. Is it okay to have a glass of wine? Can I take my Prozac? What about a Diet Coke?"

Years ago, before she knew she was pregnant, a friend of mine had a glass of wine with dinner. When she discovered she was pregnant, she worried all through her pregnancy and beyond. She feels some guilt to this day, even though the son she bore turned out very well.

Many mothers have experienced the same tangled emotions. "There's no evidence that a glass of wine a day during pregnancy has a negative impact on the developing fetus," says Dr. John Larsen, professor and chair of obstetrics and gynecology at George Washington University. Larsen says that at one time doctors gave alcohol by IV to pregnant women who were experiencing preterm labor; it relaxed the muscles and quelled contractions.

Larsen now sometimes recommends a little wine to women who experience mild contractions after a puncture from an amniocentesis needle, and some studies suggest that moderate alcohol intake in pregnancy may prevent preterm delivery in some women.

Even though most experts agree with Larsen, the alcohol message that most women hear calls for total abstinence. Experts worry that declaring moderate alcohol intake to be safe in pregnancy may encourage some pregnant women to drink immoderately. They say that pregnant women who have an occasional drink should not think they've placed their baby at risk.

What is safe? Some studies show children born to mothers who consumed three drinks a day in pregnancy averaged seven points lower on IQ tests than unexposed children. There is evidence that six drinks a day during pregnancy puts babies at risk of fetal alcohol syndrome (FAS), a constellation of serious birth defects that includes mental retardation. The higher the alcohol intake, the higher the FAS risk.

Are there drugs and drug combinations that women should avoid or take with caution during pregnancy? Accutane (isotretinoin), a prescription drug for acne and psoriasis, is known to cause birth defects. So too are some anticonvulsant drugs, including Epitol, Tegretol, and Valproate. Tetracycline, a widely prescribed antibiotic, can cause bone-growth delays and permanent teeth problems for a baby if a mother takes it during pregnancy.

Most over-the-counter drugs are considered safe in pregnancy, but some of them carry risks. Heavy doses of aspirin and other nonsteroidal anti-inflammatory drugs such as ibuprofen can delay the start of labor. They are also linked to a life-threatening disorder of newborns called persistent pulmonary hypertension (PPHN), which diverts airflow away from the baby's lungs, causing oxygen depletion. The March issue of the journal

Pediatrics published a study linking these nonprescription painkillers to PPHN, which results in the death of 15 percent of the infants who have it.

OTC DRUGS

In 1998, researchers at the University of Nebraska Medical Center reported dextromethorphan, a cough suppressant found in 40 or more OTC drugs including Nyquil, Tylenol Cold, Dayquil, Robitussin Maximum Strength, and Dimetapp DM, caused congenital malformations in chick embryos. The research was published in *Pediatric Research* and supported by the National Institutes of Health.

Although no connection between dextromethorphan and human birth defects has been shown, the Nebraska researchers noted that similar genes regulate early development in virtually all species. For this reason, the researchers predicted that dextromethorphan, which acts on the brain to suppress coughing, would have the same harmful effect on a human fetus.

Many women worry about antidepressants. Some need them during pregnancy or took them before they knew they were pregnant. A study published in the *New England Journal of Medicine* found no association between fetal exposure to antidepressants and brain damage. The study compared the IQ, temperament, activity level, and distractibility of more than 125 children whose mothers took antidepressants in pregnancy with 84 children whose mothers took no drugs known to harm the fetus.

The two groups of children, between 16 months and eight years old when tested, were comparable in every way. The antidepressants taken by the mothers included both tricyclates such as Elavil and Tofranil and selective serotonin reuptake inhibitors such as Prozac.

Not all mood-altering drugs may be safe. There is some evidence that minor tranquilizers taken for anxiety may cause developmental problems if taken in the first trimester, but there is no hard proof of this. Evidence of fetal damage caused by illegal drugs such as cocaine is widely accepted, as is the case against cigarette smoking. A 1998 survey found that 13 percent of all mothers who gave birth smoked. Evidence is striking that cigarette smoking in pregnancy lowers birth weight and increases the risks of premature birth, attention deficit hyperactive disorder, and diminished IQ.

A long-running study based on information from the National Collaborative Perinatal Project found that years after they were born, children were more apt to become addicted to certain drugs if their mother took them during delivery.

"We found drug-dependent individuals were five times more likely to have exposure to high doses of painkillers and anesthesia during their delivery than their nonaddicted siblings," says Stephen Buka of the Harvard School of Public Health. Buka suspects this is caused by a modification in the infant's brain receptors as the drugs pass from mother to child during an especially sensitive time.

CAFFEINE

Coffee consumption has worried mothers because there have been hints that caffeine may be harmful to the fetus. Like most things in life, moderation is the key. There's no evidence that 300 milligrams of caffeine a day (about three cups of coffee, or four or five cups of most regular teas, or five to six cola drinks) harms a developing baby. Higher caffeine consumption has been weakly linked to miscarriage and difficulty in conceiving.

Expectant mothers concerned about weight gain should be careful of how much of the artificial sweetener aspartame they consume. Marketed under brand names such as NutraSweet and Equal, it's found in diet soft drinks and foods.

The concern is this: In the body, aspartame converts into phenylalanine, a naturally occurring amino acid we ingest when we eat protein. At high levels, phenylalanine can be toxic to brain cells.

When we consume phenylalanine in protein, we also consume a number of other amino acids that neutralize any ill effects. When we consume it in aspartame, we get none of the neutralizing amino acids to dampen phenylalanine's impact. And as it crosses the placenta, phenylalanine's concentrations are magnified in the fetal brain.

If a fetal brain is exposed to high levels of phenylalanine because its mother consumes a lot of aspartame, will it be harmed? One study found average IQ declines of ten points in children born to mothers with a fivefold increase of phenylalanine blood levels in pregnancy. That's a lot of aspartame, and it doesn't mean an expectant mother who drinks moderate amounts of diet soda need worry.

Researchers say consuming up to three servings of aspartame a day—in either diet soda or low-calorie foods—appears to be safe for the fetus. However, a pregnant woman of average weight who eats ten or more servings a day may put her unborn baby at risk. In testimony before Congress, Dr. William Pardridge, a neuroscience researcher at UCLA, said it's likely that the effect of high phenylalanine levels in the fetal brain "will be very subtle" and many not manifest until years later.

One wild card concerns the 10 to 20 million Americans who unknowingly carry a gene linked to a genetic disease called phenylketonuria (PKU), which can lead to severe mental retardation. Most carriers don't know it, because PKU is a recessive genetic disorder, and both mother and father must carry the defective gene to pass PKU on to their child. A carrier feels no ill effects. According to researchers, a pregnant woman who unknowingly carries the PKU gene might place her unborn child at risk if she consumes even relatively moderate amounts of aspartame. There is no hard evidence that this will happen, but it remains a serious concern. PKU can be detected in the fetus by amniocentesis; a restrictive diet can prevent the worst effects of PKU on the child.

How does a mother's getting an infection affect her unborn baby? And should she be careful of cats?

Many experts think pregnant women should be more concerned about infections and household pets than a glass of wine or can of diet drink. There's overwhelming evidence of the po-

tential harm of infections during pregnancy. We've known for a long time that rubella (German measles), a viral infection, can cause devastating birth defects.

More worrisome are recent studies showing that exposure to one of the most common of winter's ills—influenza—may put an unborn child at risk of cognitive and emotional problems. If flu strikes in the second trimester, it may increase the unborn baby's risk of developing schizophrenia later in life. While the flu may be a trigger, it's likely that a genetic susceptibility is also needed for schizophrenia to develop.

Some evidence exists that maternal flu may also lead to dyslexia, and suspicions persist that a first-trimester flu may cause fetal neural-tube defects resulting in spina bifida. The common cold, sometimes confused with the flu, has not been linked to any adverse outcomes for the baby.

"Infections are probably the most important thing for a pregnant woman to protect herself against," says Lise Eliot, a developmental neurobiologist at the Chicago Medical School. "She should always practice good hygiene, like washing her hands frequently, avoiding crowds, and never drinking from someone else's cup." She adds that the flu vaccine has been approved for use during pregnancy.

Some researchers recommend that pregnant women avoid close contact with cats. Toxoplasmosis, a parasitic infection, can travel from a cat to a woman to her unborn child.

Most humans become infected through cat litter boxes. An infected woman might experience only mild symptoms, if any, so the illness usually goes undetected. If she is diagnosed with the infection, antiparasitic drugs are helpful, but they don't completely eliminate the disease. The infection is relatively rare, and the odds of passing it from mother to child are only one in five during the first two trimesters, when the fetal harm is most serious. The bad news is that a fetus infected by toxoplasmosis can suffer severe brain damage, including mental retardation and epilepsy. Some researchers also suspect it may be a latent trigger for serious mental illness as the child grows older.

CEREBRAL PALSY

An expectant mother may not realize she has potentially harmful infections. The prime suspects are infections in the reproductive tract. Researchers suspect most cerebral-palsy cases are not caused by delivery problems, as has been widely assumed. There's strong evidence that some cases of cerebral-palsy may be linked to placental infections that occur during uterine life. Other cerebral-palsy cases may be triggered by oxygen deprivation in early development, but very few appear to be caused by oxygen deprivation during delivery. It's now estimated that only 10 percent of cerebral-palsy cases are related to delivery problems.

Maternal urinary-tract infections have been linked to lower IQs in children. Another infection, cytomegalovirus (CMV), has been linked to congenital deafness. Sexually transmitted diseases such as chlamydia are suspected to be a trigger for preterm birth. Despite the serious threat posed to developing babies, infections during pregnancy remain poorly understood.

"We just don't know right now when or how the uterine infections that really make a difference to the fetus are transmitted in pregnancy," says Dr. Karin Nelson, a child neurologist and acting chief of the neuro-epidemiology branch of the National Institute of Neurologic Disorders and Stroke at NIH. "Nor do we know all the potential problems they may cause."

Because of this, researchers offer little in the way of recommendations other than clean living and careful sex. They recommend that any woman contemplating pregnancy get in her best physical condition, because a number of studies have found that a woman's general health before she becomes pregnant is vital to fetal health. They also recommend a thorough gynecological exam because it may detect a treatable infection that could harm the fetus.

Rachel Carson was right about pesticides. So if you're pregnant, how careful should you be about what you eat?

In her book *Silent Spring,* author Rachel Carson noted that when pregnant mammals were exposed to synthetic pesticides, including DDT and methoxychlor, the pesticides caused developmental abnormalities in offspring. Carson, a scientist, noted that some pesticides mimicked the female hormone estrogen and caused the male offspring to be feminized.

About the time of Carson's 1962 book, another story was emerging about diethylstilbestrol (DES), a man-made female hormone administered in the 1940s and '50s to prevent miscarriages. In the 1960s it became clear that many young daughters of DES mothers were turning up reproductive malformations and vaginal cancers. Sons born to DES mothers suffered reproductive problems, including undescended testicles and abnormal sperm counts.

ENDOCRINE DISRUPTERS

Over the years, suspicion grew from both animal and human studies that something in the environment was disrupting fetal development. In the 1990s it was given a name—endocrine disruption. The theory was that DES and the pesticides cited by Carson caused defects in offspring because they disrupted the normal endocrine process. They did this by mimicking hormones inside the human body.

It's now clear that DDT and DES are the tip of the iceberg. Today more than 90,000 synthetic chemicals are used, most made after World War II. New chemicals are produced every week. They are used in everything from pesticides to plastics.

How many of these man-made chemicals might act as endocrine disrupters? More than 50 have been identified, and hundreds more are suspects.

To understand the threat from endocrine disrupters, it helps to understand what human hormones do. Secreted by endocrine glands, these tiny molecules circulate through the bloodstream to the organs. They include estrogen, adrenalin, thyroid, melatonin, and testosterone. Each is designed to fit only into a specific receptor on a cell, like a key that fits only one lock. When a hormone connects with the cell receptor, it enters the cell's nucleus. Once there, the hormone acts as a signaling agent to direct the cell's DNA to produce specific proteins.

During fetal life, the right type and concentration of hormones must be available at the right time for normal fetal development to occur. Produced by both mother and fetus, hormones are involved in cell division and differentiation, the development of the brain and reproductive organs, and virtually everything else needed to produce a baby.

"We know from animal experiments and wildlife observations that periods in development are very sensitive to alterations in the hormone levels," says Robert Kavlock, director of reproductive toxicology for the Environmental Protection Agency.

The damage is done when chemical mimickers get into cells at the wrong time, or at the wrong strength, or both. When this happens, something in the fetus will not develop as it should.

After years of witnessing the harmful impact on wildlife, we now know that humans are not immune to endocrine disrupters. More troubling, because of the pervasiveness of these chemicals, is that we can't escape them. We get them in the food we eat, the water we drink, the products we buy.

One of the most dramatic examples came to light in the 1970s when researchers wanted to find out why so many babies born in the Great Lakes region suffered serious neurological defects. They found the answer in polychlorinated biphenyls (PCBs), organic chemicals once used in electrical insulation and adhesives. Heavy PCB contamination of Great Lakes fish eaten by the mothers turned out to be the cause.

It is not clear how PCBs cause fetal brain damage, but it's believed to happen when they disrupt thyroid hormones. Severe thyroid deficiency in pregnancy is known to cause mental retardation. Another study found reduced penis size in boys born to mothers exposed to high levels of PCBs.

The U.S. manufacture of PCBs ended in 1977. PCB levels found in the mothers and the fish they ate suggested at the time that only very high exposure caused a problem for developing babies. Now we know this isn't true.

Because PCBs don't break down, they've remained a toxin that continues to enter our bodies through the food we eat. They have leached into soil and water and are found in shellfish and freshwater fish and to a smaller degree in ocean fish. Bottom-feeding freshwater fish, such as catfish and carp, have the highest PCB concentrations.

PCBs store in fat tissue and are found in dairy products and meats. Fatty meats, especially processed meats like cold cuts, sausages, and hot dogs, are usually heaviest in PCBs. They get into these products because farm animals graze on PCB-contaminated land. However, eating fish from PCB-contaminated water remains the primary way we get these chemicals into our systems. In pregnant women, PCBs easily cross the placenta and circulate in the fetus.

PCBs are ubiquitous. They've been detected in the Antarctic snow. If you had detection equipment sensitive enough, you'd find them in the milk at the supermarket.

What concerns experts are findings from studies in the Netherlands and upstate New York that found even low maternal PCB exposures pose risk to a fetus.

The Dutch study followed 418 children from birth into early childhood. In the final month of pregnancy, researchers measured the maternal PCB blood levels, and at birth they measured PCB levels in the umbilical cord. None of the mothers was a heavy fish eater or had any history of high PCB exposure, and none of their PCB levels was considered high by safety standards.

At 3 1/2 years of age, the children's cognitive abilities were assessed with tests. After adjusting for other variables, the researchers found that maternal and cord blood PCB levels correlated with the children's cognitive abilities. As the PCB blood levels went up, the children suffered more attention problems and their cognitive abilities went down. It should be noted that the brain damage in these Dutch children was not devastating. They were not retarded or autistic. But on a relative scale, they had suffered measurable harm.

The Dutch researchers concluded that the in utero PCB exposure, and not any postnatal exposure, caused the children's brain damage. The study also revealed that these children had depressed immune function.

"All we can say now," says Deborah Rice, a toxicologist at the EPA's National Center for Environmental Assessment in Washington, "is we have strong evidence that PCB levels commonly found among women living in industrialized society can cause subtle neurological damage in their offspring." But one of the difficulties, according to Rice, is that we really don't yet know what an unsafe maternal PCB level might be.

"I think the bottom line is that women should be aware of PCBs and aware of what they're putting in their mouth," adds Rice.

The Dutch study is a warning not only about the potential impact of low levels of PCBs but about the potential harm from low levels of other endocrine disrupters.

More news arrived in March when the results from the federal government's on-going Fourth National Health and Nutrition Examination Survey (NHANES) became public. The survey of 38,000 people revealed that most of us have at least trace levels of pesticides, heavy metals, and plastics in our body tissues. In all, NHANES tested for 27 elements.

The survey found widespread exposure to phthalates, synthetic chemicals used as softeners in plastics and other products. Phthalates are one of the most heavily produced chemicals and have been linked in animal studies to endocrine disruption and birth defects. The likely sources of human exposure are foods and personal-care products such as shampoos, lotions, soaps, and perfumes; phthalates are absorbed through the skin.

Dr. Ted Schettler, a member of the Greater Boston Physicians for Social Responsibility, suspects endocrine disrupters may be linked to increases in the three hormone-driven cancers—breast, prostate, and testicular. The rate of testicular cancer among young men has nearly doubled in recent years, and the rates of learning disabilities and infertility also have increased.

"We can't blame all that is happening on toxic chemicals," says Schettler, who coauthored *In Harm's Way,* a report on how chemical contaminants affect human health. "But we need to ask ourselves if we're seeing patterns that suggest these chemicals are having a major impact on fetal development and human populations. We also need to ask what level of evidence we're

going to need before we take public-health measures. That's a political question."

The EPA's Kavlock says, "We don't know the safe or unsafe levels for many of these chemicals." Nor do we know how many of the thousands of man-made chemicals in the environment will turn out to be endocrine disrupters or cause human harm. The EPA received a mandate from Congress in 1996 to find the answers, but it will be a long wait.

"If we devoted all the toxicology testing capacity in the entire world to look for endocrine-disrupting chemicals, we couldn't do all the chemicals. There's just not enough capacity," Kavlock says. "So we are focusing on 500 to 1,000 chemicals that are the major suspects. It will take many years and a lot of money just to understand how they interact with hormonal-system and fetal development."

What is all this bad stuff we can get from eating fish or from microwaving food in plastics? Do vitamins help?

Methylmercury is a heavy metal that can cause fetal brain damage. NHANES revealed that 10 percent of American women of child-bearing age—a representative sample of all American women—had methylmercury blood and hair levels close to "potentially hazardous levels." The EPA and some nongovernment experts consider these existing methylmercury levels already above what is safe.

Dr. Jill Stein, an adolescent-medicine specialist and instructor at Harvard Medical School, has studied methylmercury's toxicity. She says the acceptable levels of methylmercury in the NHANES report were too high and that many more women are in the danger zone. "The NHANES data tells me that more than 10 percent of American women today are carrying around enough mercury to put their future children at risk for learning and behavior problems," she says.

Like PCBs and other toxic chemicals, mercury is hard to avoid because it is abundant in our environment. It comes from natural and man-made sources, chiefly coal-fired power plants and municipal waste treatment. Each year an estimated 160 tons of mercury is released into the nation's environment. In water, mercury combines with natural bacteria to form methylmercury, a toxic form of the metal. It is easily absorbed by fish. When a pregnant woman consumes the contaminated fish, methylmercury crosses the placenta and the fetal blood-brain barrier.

The world became aware of methylmercury's potential for harm more than 40 years ago in the fishing village of Minamata in Japan. People there were exposed to high levels of the heavy metal from industrial dumping of mercury compounds into Minamata Bay. The villagers, who ate a diet heavy in fish caught in the bay, experienced devastating effects. The hardest hit were the unborn. Women gave birth to babies with cerebral-palsy-like symptoms. Many were retarded.

MERCURY

Fish are the major source of mercury for humans. The Food and Drug Administration recommends that pregnant women not eat swordfish, king mackerel, shark, and tilefish. These fish are singled out because large oceangoing fish contain more methylmercury. Smaller ocean fish, especially cod, haddock, and pollock, generally have low methylmercury levels. A whitefish found off the coast of Alaska, pollock is commonly found in fish sticks and fast-food fish. Salmon have low methylmercury levels, but they are a fatty fish and apt to carry higher levels of PCBs.

Like the Dutch PCB studies, recent studies of maternal methylmercury exposure have turned up trouble. They've shown that the so-called "safe" maternal levels of the metal can cause brain damage during fetal development.

One study was carried out in the 1990s by a Danish research team that studied 917 children in the Faroe Islands, where seafood is a big part of the diet. Children were grouped into categories depending on their level of maternal methylmercury exposure; they were assessed up to age seven by neurological tests. None of the children's methylmercury exposure levels was considered high, yet many of the children had evidence of brain damage, including memory, attention, and learning problems.

"Subtle effects on brain function therefore seem to be detectable at prenatal methylmercury exposure levels currently considered safe," the study concluded. In a follow-up report published in a 1999 issue of the *Journal of the American Medical Association,* the authors said the blood concentrations of methylmercury found in the umbilical cord corresponded with the severity of the neurological damage suffered by the children.

In a study of 237 children, New Zealand researchers found similar neurological harm, including IQ impairment and attention problems, in children whose mothers' exposure to methylmercury came from fish they ate during pregnancy.

"The children in these studies were not bathed in methylmercury," notes Rita Schoeny, a toxicologist in the EPA's Office of Water. "Can people in the U.S. be exposed to the same levels of mercury in the course of their dietary practice? We think so."

Jill Stein and other experts worry that the more scientific studies we do, the more we'll realize that in fetal development there may be no such thing as a "safe" maternal level for methylmercury, PCBs, and scores of other synthetic chemicals.

"We keep learning from studies that these chemicals are harmful to fetal development at lower and lower doses," Stein says. "It's what we call the declining threshold of harm."

What about canned tuna? It has been assumed to contain low methylmercury levels because most of it comes from smaller fish. The FDA offers no advisories about it. But according to EPA researchers, a recent State of Florida survey of more than 100 samples of canned tuna found high levels of methylmercury. The more-expensive canned tuna, such as albacore and solid white tuna, usually carried higher methylmercury levels, according to the survey. This apparently is because more expensive canned tuna comes from larger tuna. In some of the canned tuna, the methylmercury levels were high enough to prevent their export to several countries, including Canada.

Some of the methylmercury levels were "worrisomely high," according to Kathryn Mahaffey, a toxicologist and director of

the division of exposure assessment at the EPA. They were high enough to cause concern for pregnant women.

"A big problem is the tremendous variability out there in the tuna supply," adds Stein. "You have no idea when you're eating a can of tuna how much methylmercury you're getting."

"Even if you ate just a small serving of some of these canned tunas each day," says Mahaffey, "you'd be substantially above a level we would consider safe."

Mahaffey and Stein agree that an expectant mother who ate even a few servings a week with methylmercury levels found in some of the canned tuna would put her developing baby at risk of brain and other neurological damage.

Now that we know a developing fetus is sensitive to even low levels of toxic chemicals, women can exercise some basic precautions to help protect their developing babies.

Don't microwave food that is wrapped in plastic or is still in plastic containers. "There are endocrine-disrupting chemicals in these plastics," Schettler says, "that leach right into the food when it's microwaved. This has been well documented and measured." Studies suggest that even at very low levels these chemicals can have an adverse effect on the fetus's hormonal system.

The EPA's Kavlock considers the fruits and vegetables you buy at the supermarket to be safe in pregnancy, but Schettler says you should try to eat organic foods to avoid even trace amounts of pesticides. Wash fruits and vegetables before eating them. Avoid pesticides or insecticide use around the house during pregnancy as well as the use of chemical solvents for painting or remodeling.

Herbicides and pesticides have leached into reservoirs that supply home drinking water, and filtration plants can't remove them all. Some are known to be endocrine disrupters. Home water filters can reduce contaminants; the best ones use active charcoal as a filtering agent.

Experts agree that a pregnant woman, or a woman who may get pregnant, can eat fish but should be careful about the kind she eats and how much of it. EPA's Rice cautions any woman who is pregnant or thinking of becoming pregnant to avoid eating any sport fish caught in a lake or river.

VEGETABLE FATS

Rice adds that the PCB risk with fish can be reduced. "Trim the fish of fat and skin, and broil or grill it," see says. "That way you cook off fat and minimize your PCB exposure." There is not much you can do to reduce the methylmercury levels in fish because it binds to protein.

"Fat is important for a baby's neurological development before and after birth, so pregnant women should consider vegetable fats like olive oil and flaxseed oil as a source," Rice adds. She says low fat dairy and meat products carry fewer PCBs than higher-fat ones.

The EPA has issued a PCB advisory for the Potomac River in the District, Virginia, and Maryland, citing in particular catsh and carp. You can go to *www.epa.gov/ost/fish/epafish.pdf* for EPA advisories on PCB and methylmercury environmental contamination. From there you can connect to state Web sites for advisories on local waters and specific fish.

Women can help prevent neurological and other birth defects by taking vitamin supplements before pregnancy. A daily dose of 400 micrograms of folic acid can reduce the risk of such problems as spina bifida by more than 70 percent as well as prevent brain defects and cleft lip and palate. Indirect evidence from a study published last year in the *New England Journal of Medicine* suggests that folic acid may also help prevent congenital heart defects.

To be effective, folic acid should be taken before pregnancy to prevent developmental defects. Folic acid comes in multivitamins and prenatal vitamins and is found naturally in legumes, whole-wheat bread, citrus fruits, fortified breakfast cereal, and leafy green vegetables. Despite the proven value of folic acid, a recent March of Dimes survey found that only 32 percent of American women of childbearing age—including pregnant women—took folic-acid supplements.

What can a fetus learn in the womb? And does playing Mozart make a baby lots smarter?

Developmental psychologist Anthony DeCasper wanted to answer two questions: What does a fetus know, and when does it know it?

DeCasper's aim was to find out if a fetus could learn in utero and remember what it learned after it was born. He enlisted the help of 33 healthy expectant mothers and asked each to tape-record herself reading passages from Dr. Seuss's *The Cat in the Hat* or from another children's book, *The King, the Mice, and the Cheese*. The mothers were randomly assigned to play one of these readings, each of which lasted two or three minutes, to their unborn children three times a day during the final three weeks of their pregnancies.

DeCasper, a professor of developmental psychology at the University of North Carolina at Greensboro, could do the experiment because it was known that fetuses could hear by the third trimester and probably earlier. DeCasper had shown earlier that at birth, babies preferred their mother's voice to all other voices. Studies in the early 1990s found that fetuses could be soothed by lullabies and sometimes moved in rhythm to their mother's voice. Fetuses hear their mother's voice from the outside, just as they can hear any other voice, but they hear the mother's voice clearer and stronger through bone conduction as it resonates inside her.

A little more than two days after birth, each of the newborns in DeCasper's study was given a specially devised nipple. The device worked by utilizing the baby's sucking reflex. When the baby sucked on the nipple, it would hear its mother's voice. But if it paused for too long a time between sucks, it would hear another woman's voice. This gave the baby control over whose voice it would hear by controlling the length of its pause between sucks.

DeCasper also placed small earphones over the infant's ears through which it could hear its mother's voice read from the books.

"Now two days or so after it was born, the baby gets to choose between two stories read by its own mother," DeCasper said. "One was the story she'd recited three times a day for the last three weeks of pregnancy, and the other is one the baby's never heard before, except for the one day his mother recorded it. So the big question was: Would the babies prefer the story they'd heard in the womb, or wouldn't they? The answer was a clear yes—the babies preferred to hear the familiar story."

DeCasper did a second experiment by having women who were not the baby's mothers recite the same two stories. The babies again showed a strong preference for the story they'd heard in the womb.

"These studies not only tell us something about the fidelity with which the fetal ear can hear," DeCasper says, "but they also show that during those two or three weeks in the womb, fetal learning and memory are occurring."

British researchers observed expectant mothers who watched a TV soap opera. The researchers placed monitors on the mother's abdomens to listen in on fetal movements when the program aired. By the 37th week of pregnancy, the babies responded to the show's theme music by increasing their movements, an indication they remembered it.

Soon after the babies were born, the researchers replayed the theme music to them. This time, instead of moving more, the babies appeared to calm down and pay attention to the music. The researchers considered this a response to familiar music.

FETAL MEMORY

"The fact that we find evidence of fetal memory doesn't mean fetuses carry conscious memories, like we remember what we ate for breakfast," explains Lise Eliot, author of *What's Going On in There?,* a book on early brain development. "But we now know there is a tremendous continuity from prenatal to postnatal life, and the prenatal experience begins to shape a child's interaction with the world it will confront after birth. Babies go through the same activity patterns and behavioral states before and after birth. Well before it is born, the baby is primed to gravitate to its mother and its mother's voice."

Some researchers speculate a baby's ability to remember in the womb may be a way of easing its transition from prenatal life to postnatal life. A baby already accustomed to and comforted by its mother's voice may be reassured as it enters a new world of bright lights, needle pricks, curious faces, and loud noises.

The question arises: Can the uterine environment affect a baby's intelligence? Twins studies have shown that genes exert an all-powerful influence on IQ. The role of environment in IQ has traditionally meant the nurturance and stimulation the baby receives after birth.

Bernie Devlin, a biostatistician and assistant professor of psychiatry at the University of Pittsburgh, did an analysis of 212 twins studies on intelligence. In a paper published in *Nature,* he concluded that the accepted figure of 60 to 80 percent for IQ heritability is too high. It should be closer to 50 percent, he says, which leaves more room for environmental factors. Devlin says the one environmental factor that's been missing in understanding human intelligence is time in the womb.

"I'm surprised that the impact of fetal life on a child's intelligence had not been accounted for in these IQ studies," Devlin says. "I know it's very complicated, but it's surprising that people who study the heritability of intelligence really haven't considered this factor."

What is the impact of life in the womb on intelligence? Devlin thinks it's equal to if not greater than the impact of a child's upbringing. In other words, it's possible a mother may have more influence over her child's intelligence before birth than after.

As the brain develops in utero, we know it undergoes changes that affect its ultimate capacity. Nutritional and hormonal influences from the mother have a big impact. And twins studies show that the heavier twin at birth most often has the higher IQ.

A number of studies from the United States and Latin America also found that a range of vitamins, as well as sufficient protein in the mother's prenatal diet, had an impact on the child's intelligence.

Links between specific vitamins and intelligence have been borne out in two studies. An animal study conducted at the University of North Carolina and published in the March issue of *Developmental Brain Research* found that rats with a choline deficiency during pregnancy gave birth to offspring with severe brain impairments. Choline, a B-complex vitamin involved in nerve transmission, is found in eggs, meat, peanuts, and dietary supplements.

The August 1999 issue of the *New England Journal of Medicine* reported that expectant mothers with low thyroid function gave birth to children with markedly diminished IQs as well as motor and attention deficits. The study said one cause of hypothyroidism—present in 2 to 3 percent of American women—is a lack of iodine in the American diet. Women whose hypothyroidism was detected and treated before pregnancy had children with normal test scores. Hypothyroidism can be detected with a blood test, but expectant mothers who receive little or late prenatal care often go undiagnosed or are diagnosed too late to help their child.

Although most American women get the nutrition they need through diet and prenatal vitamins, not all do. According to a National Center for Health Statistics survey, more than one in four expectant mothers in the U.S. received inadequate prenatal care.

Devlin's *Nature* article took a parting shot at the conclusions reached in the 1994 book *The Bell Curve,* in which Richard J. Herrnstein and Charles Murray argued that different social classes are a result of genetically determined, and therefore unalterable, IQ levels. The lower the IQ, the argument goes, the lower the social class.

Not only does the data show IQ to be far less heritable than that book alleges, Devlin says, but he suspects improvements in the health status of mostly poor expectant mothers would see measurable increases in the IQs of their offspring.

Devlin's argument is supported by Randy Thornhill, a biologist at the University of New Mexico. Thornhill's research suggests that IQ differences are due in part to what he calls "heritable vulnerabilities to environmental sources of developmental stress." In other words, vulnerable genes interact with

environmental insults in utero resulting in gene mutations that affect fetal development. Thornhill says environmental insults may include viruses, maternal drug abuse, or poor nutrition.

"The developmental instability that results," Thornhill says, "is most readily seen in the body's asymmetry when one side of the body differs from the other. For example, on average an individual's index fingers will differ in length by about two millimeters. Some people have much more asymmetries than others."

But the asymmetries we see on the outside also occur in the nervous system. When this happens, neurons are harmed and memory and intelligence are impaired. Thornhill says the more physical asymmetries you have, the more neurological impairment you have. He calculates that these factors can account for as much as 50 percent of the differences we find in IQ.

Thornhill adds that a fetus that carries these genetic vulnerabilities, but develops in an ideal uterine environment, will not experience any serious problems because the worrisome mutations will not occur.

"The practical implications for this are tremendous," Thornhill says. "If we can understand what environmental factors most disrupt fetal development of the nervous system, then we'll be in a position to remove them and have many more intelligent people born."

Studies on fetal IQ development suggest that the current emphasis on nurturance and stimulation for young children be rethought. The philosophy behind initiatives such as Zero to Three and Early Head Start makes sense. The programs are based on evidence that the first three years are very important for brain development and that early stimulation can effect positive changes in a child's life. But Devlin and Thornhill's research suggests a stronger public-health emphasis on a baby's prenatal life if we are to equalize the opportunities for children.

Does that mean unborn babies need to hear more Mozart? Companies are offering kits so expectant mothers can play music or different sounds to their developing babies—the prenatal "Mozart effect." One kit promises this stimulation will lead to "longer new-born attention span, better sleep patterns, accelerated development, expanded cognitive powers, enhanced social awareness and extraordinary language abilities." Will acceptance to Harvard come next?

"The number of bogus and dangerous devices available to expectant parents to make their babies smarter constantly shocks me," says DiPietro. "All these claims are made without a shred of evidence to support them."

Adds DeCasper: "I think it is dangerous to stimulate the baby in the womb. If you play Mozart and it remembers Mozart, is it going to be a smarter baby? I haven't got a clue. Could it hurt the baby? Yes, I think it could. If you started this stimulation too early and played it too loud, there is evidence from animal studies that you can destroy the ear's ability to hear sounds in a particular range. That's an established fact. Would I take a risk with my fetus? No!"

DeCasper and other researches emphasize that no devices or tricks can enhance the brainpower of a developing baby. Their advice to the expectant mother: Take the best possible care of yourself.

"The womb is a quiet, protective place for a reason," DiPietro concludes. "Nature didn't design megaphones to be placed on the abdomen. The fetus gets all the stimulation it needs for its brain to develop."

Mr. Pekkanen is a contributing editor to The Washingtonian. *From "Secrets of the Womb," by John Pekkanen,* The Washingtonian, *August 2001, pages 44–51, 126–135.*

From *Current*, September 2001, pp. 20-29.

HHG-4M

The Mystery of Fetal Life article
Pekkanen, J. (2001)

Answer the following questions with reference to the above article.

1. Does a fetus breathe? How?

2. How soon into the pregnancy do the earliest brain tissues begin to form?

3. How long does it take for the brain to develop?

4. Which of the senses are in place during the pregnancy?

5. Who is responsible for the release of hormones to begin the labour process (mother or baby)?

6. What is the safe level of alcohol consumption for pregnant women?

7. How does alcohol consumption affect a developing fetus?

8. Generally, how do over the counter medications like Ibuprofen, Nyquil, Tylenol, Robitussin, Dimetapp affect a developing fetus?

9. What is the best advice for pregnant moms regarding caffeine consumption?

10. What is PKU? What causes it? How does it affect developing fetuses?