

OB/GYN Clinical [ALERT]

Evidence-based commentaries
on women's reproductive health

ABSTRACT & COMMENTARY

Eat More Fish? Choose Fish Carefully to Avoid Mercury Toxicity

By *John C. Hobbins, MD*

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Dr. Hobbins reports no financial relationships relevant to this field of study.

SYNOPSIS: A recent review deals with the benefits, as well as the risks, of eating fish rich in omega-3 fatty acids and pinpoints which fish contain the most and least amounts of mercury.

SOURCE: Wenstrom KD. DEA's new advice on fish: It's complicated. *Am J Obstet Gynecol* 2014;211:475-478.

The December issue of the *American Journal of Obstetrics and Gynecology* contained a commentary by Katharine Wenstrom on the FDA's "newest advice on fish."¹ It is so well done that I thought that this month, for the first time, I would review a review.

In June 2014, the FDA and the Environmental Protection Agency (EPA) came out with a recommendation entitled "New advice: Some women and young children should eat more fish."² Those reading the article just may be off to the market immediately! Well, not so fast. Unfortunately, the report has a dark side. This document and other sources indicate that women should be very selective with

their fish choices, since some may not be safe to eat in pregnancy, even in modest amounts.

First, the benefits of fish: Fish contain varying amounts of omega-3 fatty acids, which have anti-inflammatory properties and are intimately involved at the cellular level in enzyme function and neurotransmission.³ In short, they are essential components in the development of the fetal brain and even the retina. Studies have also shown that they are major players in cardiac development and function.⁴ For these and other reasons, the FDA recommends that pregnant women eat between 8-12 ounces of fish per week.²

Discussions involving the benefits of omega-3 fatty acids

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and fish eating, in general, concentrate on two major components: docosapentaenoic acid (DHA) and eicosapentaenoic acid (EPA). Part of the American Heart Association's "heart healthy diet,"⁵ both have been touted as being necessary for normal development of the fetal central nervous system.⁶ Studies have shown that eating at least 340 g of "fatty" fish a week containing DHA and EPA may decrease the rate of preterm birth,⁷ increase birth weight,⁸ and improve childhood IQs.⁹

Now to the dark side: Many fish whose flesh is rich in omega-3 fatty acids are also rich in organic methyl mercury and, in some cases, the evil pollutants, dioxin, and polychlorinated biphenyls (PCBs). Mercury can negate many of good things that the omega-3 fatty acids offer, so the pregnant (and even non-pregnant) fish eater needs to be well-informed. In fact, some studies, such as ones from the Faroe Islands¹⁰ and Seychelles,¹¹ suggest that neurotoxicity can be linked to diets that rely heavily on some types of fish. The most common symptoms of methyl mercury toxicity are paresthesias, peripheral vision problems, ataxia, and memory loss.

Not surprisingly, we are responsible for this. Most methyl mercury in fish comes from the burning of coal, with small particles being spewed into the air, often travelling far away from their origin. For example, cobia and grouper from Key West (where the only nearby fires are in the pizza ovens) contain high amounts of mercury. Mercury gets into minute forms of marine life, and this plankton is a major food source for smaller marine creatures who are eaten by larger fish. They, in turn, are eaten by the even larger prowling predator fish that we humans love to consume.

Dioxin and PCB, which come from industrial and agricultural fallout, are found in high concentrations in many fish in the Great Lakes or rivers close to factories or agricultural runoff. Like mercury, these pollutants have the capacity to hang around forever, and no amount of dilution in the vast seas can now prevent the continual accumulation, especially in the large predators who steadily concentrate pollutants throughout their longer life span.

Ideally, this *Alert* should have the entire list

of commonly consumed fish along with their DHA, EPA, and mercury concentrations, but this would take up too much room. However, the *Gray Journal* review¹ has just such a table — one I would recommend putting up on the wall in your consultation area and/or incorporate into a handout for pregnant patients.

Briefly, the fish to limit or avoid are: swordfish, king mackerel, tuna, shark, bluefish, marlin, and tile fish. Even some lobsters, who can live for 20 years, are in the "moderate to high" category.

Those with the lowest level of mercury are shellfish (clams, mussels, oysters, scallops, and crab) and small wild fish (sole, flounder, anchovies, and sardines). Also, pollack (think fish sticks), as well as *some* farm-raised fish, such as domestic tilapia, catfish, and striped bass, have low mercury levels. The winner that gives the lowest mercury and highest DHA and EPA benefit is wild Pacific salmon. Shrimp has the very lowest levels of mercury but, alas, it has virtually no omega-3 fatty acids. Sadly, Atlantic cod and salmon, while having low mercury levels, are in danger of extinction (again, our bad).

■ COMMENTARY

First: a personal note. For years, my wife and I have been eating a wide variety of fish for 5-8 meals a week, especially when we are in Key West. Her interest in mercury was tweaked by an article in *Consumer Reports*, so, for reassurance, she got her blood tested for mercury about 3 months ago. The EPA advises that individuals with levels < 5 ug/L are okay, but any individual with a level > 10 ug/L is considered to be "poisoned." Hers was 22. I followed suit and mine was 33. We then began consuming only fish that had little or no mercury according to EPA tables. After 2.5 months her level is now 9 and mine is down to 16. It is ironic that the first article I ever wrote was in *Contemporary OB/GYN* on mercury-related birth defects from chemical dumping into Minamata Bay, Japan. Now, four decades later, I am theoretically poisoned by it.

Yes, much of the information that is online could be labeled as smoke and mirrors, but methyl mercury contamination of fish is *real* and could be detrimental to a developing fetus. But, unfortunately, bypassing the unwanted components in fish by going

directly to fish oil products, or even to supplements labeled as DHA and EPA, may not do the job. A Cochrane meta-analysis of randomized trials suggests little benefit from the sanitized versions.⁸ One apparently benefits mostly from what the FDA considers “the whole package.”

To further complicate the discussion, there has been some controversial online chatter regarding the theory that methyl mercury interferes with the action of selenium in important enzyme systems through a pathway that also involves sulfur. However, it is unclear if mercury causes damage by antagonizing the inherent beneficial effects of selenium or whether the selenium is protective by blocking the evil effects of methyl mercury. Since fetuses have no real stores of selenium, the mercury will be unopposed in the central nervous system, making their brains particularly vulnerable. Theoretically, the more selenium one has in his/her circulation and/or ingests (Brazil nuts are a good source, and, of course, fish), the less potential harm the mercury can do at the cellular level.

Selenium or no selenium, it is clear that there is enough evidence to indicate that 8-12 ounces of fatty fish per week can have a major health benefit to pregnant women and may be essential for their fetuses. If someone likes shrimp, have at it, but do not expect any real bump in omega-3 fatty acid levels. If your patients like swordfish or tuna and are pregnant, they might have to wait until after pregnancy to eat it with any frequency. Wild Pacific salmon seems to have the best balance between DHA, EPA, selenium (all high), and methyl mercury (very low). I have not seen this recommendation anywhere else, but I would suggest that patients who are very frequent fish eaters and wish to become pregnant have a blood test for mercury. If high, it would be wise to attempt to drop

the levels to reasonable range before becoming pregnant. If levels are within acceptable limits, then the maternal blood levels should remain in tolerable range if maternal intake of mercury is controlled. Patients wishing to monitor their daily mercury intakes through a mercury calculator can visit the National Resources Defense Council (NRDC) web site at: www.nrdc.org/health/effects/mercury/calculator/start.asp. ■

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ABSTRACT & COMMENTARY

Robotic-assisted Adnexal Surgery: More Complications and Higher Cost

By Jeffrey T. Jensen, MD, MPH

SYNOPSIS: The performance of robotically assisted adnexal surgery increased dramatically over the last decade. Compared with standard laparoscopic surgery, intraoperative complications and costs are substantially higher.

SOURCE: Wright JD, et al. Comparative effectiveness of robotically assisted compared with laparoscopic adnexal surgery for benign gynecologic disease. *Obstet Gynecol* 2014;124:886-896.

The authors used Perspective, a national database from the United States, to evaluate trends in adnexal surgery in gynecology. This database captures clinical and demographic data, procedures, and other hospital services from more than 500 acute care

hospitals throughout the United States, approximately 15% of all hospitalizations. Subjects were women ages 18 years or older who underwent laparoscopic or robotic oophorectomy or ovarian cystectomy (without hysterectomy) for benign disease between 2009-2012.

The perioperative morbidity and mortality, resource use, and costs were compared between the two approaches. To limit the influence of confounding on the choice of surgical approach, a propensity score-matched analysis was performed to provide adjusted odds ratios (ORs). Additional sensitivity analyses were performed that limited the comparison to patients with endometriosis only and to procedures performed only by high-volume surgeons.

A total of 87,514 procedures were identified. During the study period, use of robotic-assistance increased from 3.5% (oophorectomy) and 2.4% (cystectomy) in 2009 to 15% and 12.9% in 2012, respectively. While there was no difference in the overall complication rate, the intraoperative complication rate was significantly higher for both oophorectomy (3.4% vs 2.1%; OR, 1.6; 95% confidence interval [CI], 1.21-2.13) and cystectomy (2.0% vs 0.9%; OR, 2.4; 95% CI, 1.31-4.38). The cost

["The bottom line is the robotic approach is \$2500 higher for oophorectomy and more than \$3000 higher for ovarian cystectomy. Who is paying for this and why?"]

of the robotic procedures was also significantly higher (mean total addition \$2504, 95% CI, \$2356-2652 for oophorectomy; and \$3310, 95% CI, \$3082-3581 for cystectomy). Propensity matching and restriction of the analysis to complicated cases (endometriosis) or those performed by high-volume surgeons did not change the findings. Although obesity was not specifically considered in these adjustments, the authors did use the Elixhauser comorbidity index, a coding algorithm used to assess comorbidities in large administrative databases to adjust for high-risk patients. This index includes obesity, diabetes, and a number of other factors related to poor surgical outcomes.

■ COMMENTARY

Gynecologic surgeons are under enormous pressure to adopt minimally invasive techniques to attract a diminishing volume of surgical cases. In the 1990s, the explosion of technology for advanced laparoscopic surgery powered widespread adoption of a surgical technique that transformed the specialty. These advances improved the care of women and changed the standard approach for surgical evaluation of an adnexal mass from a midline incision and 4-day postoperative stay to

three laparoscopic 5-10 mm incisions and day surgery. Costs decreased primarily as a result of the decreased hospital stay. Women recovered faster and benefited greatly through the advance in technology.^{1,2}

The past decade has seen a similar shift toward robotic-assisted surgery. Robotics offer several advantages to surgeons, including more favorable ergonomics and intuitive surgical motion with "wristed" instruments. These advantages have resulted in advances in care for pelvic reconstructive surgery and gynecologic oncology, where procedures like sacrocolpopexy and radical hysterectomy are routinely performed using a minimally invasive technique.

But marketing of the robot by hospitals and surgeons appears to have driven the overuse of this technology in benign gynecology to include procedures like hysterectomy that should be considered by the more minimally invasive approach of vaginal surgery. The use of the robot for adnexal surgery appears to be another overreach.

The study by Wright et al used a large validated database of representative insurance claims from the United States to evaluate outcomes from laparoscopic and robotic adnexal surgery. The finding that the proportion of adnexal surgery performed robotically increased by more than 10% during the 3-year study period is remarkable. More remarkable is the lack of benefit to patients. While the risk of intraoperative complications was two-fold higher in robotic cases, the overall chance of a complication was small with both approaches. But even if we ignore this potential for harm, at best there appears to be no difference in outcomes between straight-stick laparoscopy and the robot. This would be fine if the robot provided other benefits over standard laparoscopy, but this does not appear to be true for adnexal surgery. Both procedures are commonly performed as outpatient surgery. In most cases, the incision size and placement are smaller and more cosmetic with standard laparoscopy. The authors conducted sensitivity analyses and determined the results were the same if only high-volume surgeons or complex cases were considered. The bottom line is the robotic approach is more expensive — \$2500 higher for oophorectomy and more than \$3000 higher for ovarian cystectomy. Who is paying for this and why?

Some surgeons see using the robot for adnexal cases as a strategy to increase their robot experience and skill for more complex cases. But copays under many health insurance plans run between 20-40% for outpatient surgery. Do patients benefit from this additional \$500-1000 in out-of-pocket costs? And if the goal is to increase skills to perform robotic-assisted hysterectomy, the logic seems even fuzzier.

I picked up a book from the giveaway pile at our library — a 1957 edition of *Cope's Early Diagnosis of the Acute Abdomen*. The detailed description of signs and symptoms to consider in evaluation of the acute abdomen is a classic. The decision to operate is significant and must always be guided by the principle to “first do no harm.” I wonder about the trends in modern medicine. Will physical diagnosis and common sense both be abandoned as we route patients directly from the

CT scanner to a date with a robotic surgeon? ■

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ABSTRACT & COMMENTARY

Is Pregnancy a Risk Factor for Future Obesity?

By *Rebecca H. Allen, MD, MPH*

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Dr. Allen reports she is a retained consultant for Bayer.

SYNOPSIS: In this prospective cohort study, being overweight or obese pre-pregnancy and excessive weight gain during pregnancy were associated with postpartum weight retention (> 20 pounds) at 1 year. Protective factors were breastfeeding at 6 months and moderate exercise.

SOURCE: Endres LK, et al. Postpartum weight retention risk factors and relationship to obesity at 1 year. *Obstet Gynecol* 2015;125:144-152.

This is a nested prospective cohort study of 774 women who were participants in the multi-site Community Child Health Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Sites of recruitment included Baltimore, Los Angeles, Washington, DC, Lake County, Illinois, and eastern North Carolina. The main study enrolled women ages 18-40 years with a live birth at 20 weeks' gestation or longer. Women who could not or were unlikely to become pregnant again in the future were excluded (those who underwent postpartum sterilization or had four or more children). This sub-study included those women who had pre-pregnancy height and weight data available and weight data at 1 year postpartum without a subsequent pregnancy in that year. Body mass index (BMI) was calculated and used standard Institute of Medicine (IOM) definitions (underweight < 18.5 kg/m², normal weight 18.5-24.9 kg/m², overweight 25.0-29.9 kg/m², and obese 30.0 kg/m² or higher). There was no difference between the women eligible for the sub-study and the 1736 women who were excluded in terms of age, race, parity, or income level. Other data collected included insurance, education, exercise, breastfeeding, smoking, and sleep.

The mean age of the study population was 26 (± 5.8) years and one-third of the women were enrolled after having their first child. Approximately, one-half of the sample reported African American race, one-quarter Hispanic, and one-quarter white. Pre-pregnancy, 4% of the women were underweight, 40% normal weight, 26% overweight, and 30% obese. At 1 year postpartum,

among women who were normal weight before pregnancy, 30% became overweight and 2% obese. Among women who were overweight pre-pregnancy, 44% became obese by 1 year postpartum. In fact, 75% of the women were heavier at 1 year postpartum than pre-pregnancy. Half of the sample gained more than the recommended amount of weight gain during pregnancy per IOM guidelines. In multivariate analysis, excessive weight gain during pregnancy (odds ratio [OR], 1.08; 95% confidence interval [CI], 1.06-1.10) and pre-pregnancy BMI (overweight OR, 3.25; 95% CI, 1.90-5.55; obese OR, 3.72; 95% CI 2.17-6.38) increased the

[“...women deserve to hear the recommended guidelines for weight gain in pregnancy, and weight should be monitored at each prenatal visit.”]

odds of excessive weight retention (> 20 lbs or more) at 1 year postpartum while breastfeeding at 6 months (OR, 0.46; 95% CI, 0.24-0.87) and moderate exercise (OR, 0.61; 95% CI, 0.40-0.93) was protective.

■ COMMENTARY

More than one-third (78.6 million) of adults in the United States are obese,¹ a major public health problem. Pregnancy and its accompanying “baby weight”

have long been suspected to be a risk factor for future weight gain and obesity. Obesity puts women at risk for pregnancy complications as well as for their lifelong health in terms of cardiovascular disease, diabetes, and osteoarthritis.² During pregnancy, health care providers should counsel women on the IOM guidelines for weight gain, which are categorized by pre-pregnancy BMI.³ For singleton pregnancies, these guidelines state that underweight women should gain no more than 28-40 lbs, normal weight women 25-35 lbs, overweight women 15-25 lbs, and obese women 11-20 lbs, respectively, during pregnancy. Some trials have shown success in limiting gestational weight gain with combining physical activity and diet counseling during pregnancy. One meta-analysis indicated that this approach reduced gestational weight gain by 1.2 kg (2.6 lbs), where the mean gestational weight gain was 13 kg (28 lbs).⁴

The authors of this study confirm that pre-pregnancy BMI and excessive weight gain during pregnancy are risk factors for postpartum weight retention at 1 year. Women who do not return to their pre-pregnancy weight postpartum are at risk of becoming more overweight with every pregnancy in their lifetime. While the source of the study population was mostly low-income, by design, it was racially diverse and the results are likely generalizable. Some limitations of the study include breastfeeding assessment, which could not distinguish between partial and exclusive breastfeeding, and the fact that physical activity was self-reported. Nevertheless, the variables that remained predictive in multivariable analysis make biologic sense.

The American College of Obstetricians and Gynecologists recommends the following for overweight or obese women considering pregnancy or who are pregnant.⁵

- Preconception assessment and counseling are strongly encouraged and should include the provision of specific information concerning the

maternal and fetal risks of obesity in pregnancy and encouragement to undertake a weight-reduction program.

- At the initial prenatal visit, height and weight should be recorded for all women to allow calculation of BMI, and recommendations for appropriate weight gain, guided by IOM recommendations, should be reviewed both at the initial visit and periodically throughout pregnancy.
- Nutrition consultation should be offered to all overweight or obese women, and they should be encouraged to follow an exercise program. Nutrition and exercise counseling should continue postpartum and before attempting another pregnancy.

While these recommendations may be difficult to incorporate into a busy practice, women could be referred to a nutritionist and/or weight loss program. At the very least, women deserve to hear the recommended guidelines for weight gain in pregnancy and weight should be monitored at each prenatal visit. There is even research suggesting that obese women may not need to gain any weight in pregnancy at all.⁶ This is an area that is changing rapidly and it may be that the IOM changes its recommendations in the future. ■

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ABSTRACT & COMMENTARY

Cervical Cancer Screening: Are We Going in the Wrong Direction?

By Robert L. Coleman, MD

Professor, University of Texas; M.D. Anderson Cancer Center, Houston

Dr. Coleman reports no financial relationships relevant to this field of study.

SYNOPSIS: Cervical cancer screening in the United States is underpacing targets to meet the Healthy People 2020 objectives of 93% compliance with guidelines. While overall incidence rates of cervix cancer have decreased slightly, mortality has not, and underserved, underinsured, and minority/ethnic populations continue to be at highest risk for cervical cancer development.

Significant effort and progress has been made in cervical cancer screening in the United States, with dramatic effects on cancer burden. However, the disease continues to be diagnosed, with highest risks for late-stage diagnosis and death observed in under-resourced demographics and individuals. As part of an ongoing evaluation of disease burden, the authors from the Centers for Disease Control and Prevention surveyed (by phone) 133,851 women across all 50 states and the District of Columbia to ascertain cervical cancer screening rates over a 5-year period (2007-2011). Outcome measures were cervical cancer incidence and mortality, current screening percentages, factors associated with higher incidence and death rates, and inadequate screening. Percentages of women who had not been screened for cervical cancer in the past 5 years were estimated using data from the 2012 Behavioral Risk Factor Surveillance System survey. The sample, consisting of women ages 21-65 years who had complete Pap data and no hysterectomy, corresponded to a U.S. population of more than 70 million at-risk women. In 2012, 8.2 million women (11.4%) had not been screened for cervical cancer in the past 5 years. The percentage was larger for women without health insurance (23.1%) and for those without a regular health care provider (25.5%). From 2007 to 2011, the cervical cancer incidence rate decreased by 1.9% per year, while the death rate remained stable. Geographically, Southern states, such as New Mexico, Texas, Oklahoma, Louisiana, and Mississippi, had the highest incidence rate (8.5 per 100,000), death rate (2.7 per 100,000), and percentage of women who had not been screened in the past 5 years (12.3%). The proportion of inadequately screened women was higher among older women, Asians/Pacific Islanders, and American Indians/Alaska Natives. The authors conclude that despite well-described and disseminated screening guidelines, there continue to be women who are not screened as recommended. Efforts to improve catchment are required to meet the Healthy People 2020 (HP2020) targets.

■ COMMENTARY

There are few “wins” in the cancer business. Period. However, if there ever was a poster child for an intervention that can dramatically impact the natural trajectory of cancer development and saving lives, it’s the Pap smear. This simple test was introduced into the public domain (to some notable resistance) in the late 1940s, and outside of the addition of some processing improvements and HPV genomics, the test has remained largely unchanged since that time.¹ It’s effective, not only in identifying at-risk or affected women with cervix pathology, but also in reducing the rate of incurable or highly advanced disease requiring extensive, expensive, and morbid treatment. These facts are overt

and reproducible. Thus, this report is nothing short of distressing; and it’s probably worse than presented, as this survey was limited to those women reachable by phone. While prevalence rates were limited to those with a uterus, the incidence rates of cancer were not adjusted for prior hysterectomy. When one also acknowledges the poor uptake of preventive vaccination (38% in girls, 14% in boys), it’s not surprising greater progress to the HP2020 goals have not been made.^{2,3}

Nevertheless, these survey data, by state, are informative and can be used as powerful leverage to individually resource initiatives impacting public health. The emergence and implementation of the Affordable Care Act has led to historically low rates of uninsured Americans, which in addition to the availability of free cancer screening through the National Breast and Cervical Cancer Early Detection Program,⁴ provides hope for greater compliance with accepted guidelines. In addition, for the first time in 2012, all national screening organizations, including the U.S. Preventive Services Task Force, the American Cancer Society, and the American College of Obstetrics and Gynecology, have come to consensus on when and how often women should be screened for cervical cancer.⁵ As new technology and age-dependent screening recommendations emerge, consensus messaging will be necessary to maintain traction to meet the HP2020 target of 93% compliance. ■

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CME QUESTIONS

1. Which type of fish has the lowest mercury level?
a. Tuna
b. Grouper
c. Salmon
d. Swordfish
2. Since mercury has a short life, avoiding mercury-containing fish should result in a rapid return to normal in those with previously high mercury blood levels.
a. True
b. False
3. Compared to standard laparoscopic approaches, robotic-assisted adnexal surgery has resulted in:
a. a decrease in hospital stays.
b. a decrease in intraoperative complications.
c. an improvement in patient acceptability.
d. an increase in cost.
4. In the study by Endres et al, postpartum weight retention was common with the majority of the women weighing more at 1 year postpartum compared to pre-pregnancy.
a. True
b. False
5. Which of the following is a noted limitation to the cervical cancer screening survey methodology?
a. Not all 50 U.S. states were represented.
b. The survey did not adjust cancer incidence and mortality rates to those women who have not undergone hysterectomy.
c. It included women reachable by cell phone or landlines.
d. It oversampled the Southern states.

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- Explain the latest data regarding diagnosis and treatment of various diseases affecting women;
- Discuss new data concerning prenatal care, neonatal health, and complications arising in pregnancy and the perinatal period; and
- Discuss the advantages, disadvantages, and cost-effectiveness of new testing procedures in women's health.

[IN FUTURE ISSUES]

Update on Postoperative Delirium in Older Adults:
Best Practice Statement from the American Geriatrics Society

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