Class 3 Handout

http://www.alternamoms.com/ultrasound.html

ON THE "SAFETY" AMD "USEFULNESS" OF PRENATAL ULTRASOUND

Ultrasound May Change Baby's Cell Growth
June 9, 1999 (from CNN.com) Web posted at: 3:10 PM EDT (1910 GMT)

LONDON (Reuters) -- Ultrasound scans, routinely used to look at internal organs and to monitor the growth of a developing fetus, can stop cells from dividing normally, Irish scientists said Wednesday.

Researchers at University College in Dublin told New Scientist magazine it is too early to tell if the changes they found in the cells of mice are harmless or what the implications of the findings could be for humans.

"It has been assumed for a long time that ultrasound has no effect on cells," said Patrick Brennan, who led the research team. "We now have grounds to question that assumption."

During the study, the rate of cell division in mice that were given an 8 megahertz scan lasting 15 minutes was 22 percent lower than normal, and the rate of cell death doubled.

Routine hospital scans use frequencies between 3 and 10 megahertz and can last up to 60 minutes.

Brennan said the sound waves of the scans could be damaging the DNA in cells, which could delay cell division and repair, or it might be switching on p53, a tumor suppressor gene that controls cell death.

Cancer occurs when damaged cells multiply uncontrollably and form tumors. Mutations in p53 are the commonest gene abnormalities seen in human cancers.

"Our results are preliminary and need further investigation," Brennan told the magazine.

Shadow of a Doubt <http://www.newscientist.com/ns/19990612/newsstory12.html>
by Rob Edwards, from New Scientist, 12 June 1999

ULTRASOUND SCANS can stop cells from dividing and make them commit suicide. A research team in Ireland say this is the first evidence that routine scans, which have let doctors peek at fetuses and internal organs for the past 40 years, affect the normal cell cycle.

A team led by Patrick Brennan of University College Dublin gave 12 mice an 8-megahertz scan lasting for 15 minutes. Hospital scans, which reflect inaudible sound waves off soft tissue to produce images on a monitor, use frequencies of between 3 and 10 megahertz and can last for up to an hour.

The researchers detected two significant changes in the cells of the small intestine in scanned mice compared to the mice that hadn't been scanned. Four and a half hours after exposure, there was a 22 per cent reduction in the rate of cell division, while the rate of programmed cell death or "apoptosis" had approximately doubled.

Brennan believes there will be similar effects in humans. "It has been assumed for a long time that ultrasound has no effect on cells," he says. "We now have grounds to question that assumption."

Brennan stresses, however, that the implications for human health are uncertain. "There are changes happening, but we couldn't say whether they are harmful or harmless," he explains. The intestine is a very adaptable organ that can compensate for alterations in the cell cycle, says Brennan.

It is possible that the sound waves damage the DNA in cells, delaying cell division and repair. Brennan suggests that ultrasound might be switching on the p53 gene which controls cell deaths. This gene, dubbed "the guardian of the genome", produces a protein that helps cells recognise DNA damage and then either self-destruct or stop dividing.

Studies in the early 1990s by researchers at the University of Rochester in New York and the Batelle Pacific Northwest Laboratories in Richland, Washington, showed that tissue heating due to ultrasound can cause bleeding in mouse intestines. Ultrasonographers now tune the power of scans to reduce such heating.

But Brennan's work is the first evidence that scans create changes in cells. "Our results are preliminary and need further investigation," he says. The team presented their results at the Radiology 1999 conference in Birmingham last month and are now preparing them for submission to a peer-reviewed journal.

Alex Elliott, a researcher in clinical physics at the University of Glasgow, thinks that Brennan's results are important and should be followed with further studies. "If the conditions of his experiments really compare to the clinical use of ultrasound," he says, "we may have to review the current safety limits."

Newnham, J.P., Evans, S.F., Michael, C.A., Stanley, F.J., & Landau, L.I. (1993). Effects of Frequent Ultrasound During Pregnancy: A Randomized Controlled Trial. The Lancet, 342(Oct.9), 887-891.

A study of over 1400 women in Perth, Western Australia compared pregnant mothers who had ultrasound only once during gestation with mothers who had five monthly ultrasounds from 18 weeks to 38 weeks. They found significantly higher intrauterine growth restriction in the intensive ultrasound group. These mothers gave birth to lower weight babies.

The researchers concluded that prenatal ultrasound imaging and Doppler flow exams should be restricted to clinically necessary situations. This recommendation comes at a time when ultrasound during prenatal visits has become increasingly popular and serves as a kind of entertainment feature of office check-up visits.

Campbell, J.D., Elford, R.W. & Brant, R.F. (1993). Case-Controlled Study of Prenatal Ultrasound Exposure in Children with Delayed Speech. Canadian Medical Association Journal, 149(10), 1435-1440.

Delayed speech is not a pathological or organic syndrome but developmentally defined symptom complex. Clinicians have noted an increased incidence of delayed speech in pediatric patients.

This is a matched-case control study of 72 children 2 to 8 years old presenting with delayed speech of unknown cause. The children were measured for articulation, language comprehension, language production, meta-linguistic skills, and verbal memory. When checked for ultrasound exposure, the speech-delayed children were about twice as likely to have been

exposed to ultrasound than the matched controls.

The authors believe that delayed speech is a sensitive measure reflecting sub-optimal conditions for development. If ultrasound can cause developmental delays, the authors are concerned about the routine use of ultrasound and they warn against it.

Devi, P.U., Suresh, R., & Hande, M.P. (1995). Effect of fetal exposure to ultrasound on the behavior of the adult mouse. Radiat Res (QMP), 141(3), 314-7.

Pregnant Swiss albino mice were exposed to diagnostic ultrasound. There were significant alterations in behavior in all three exposed groups as revealed by the decreased locomotor and exploratory activity and the increase in the number of trials needed for learning. These results indicate that ultrasound exposure during the early fetal period can impair brain function in the adult mouse.

Hande, M.P., & Devi, P.U. (1995). Teratogenic effects of repeated exposures to X-rays and/or ultrasound in mice. Neurotoxicol Teratol (NAT), 17(2), 179-88.

Pregnant Swiss mice were exposed to ultrasound, x-rays, and combinations of the two. Effects on
prenatal development, postnatal growth and adult behavior were studied. U + U group showed an increase in percent growth retarded fetuses. The postnatal mortality was significantly higher only in the U + U group. In the X + U group, the exploratory activity was affected at 6 months of age. There was a significant change in the locomotor activity with a reduction in the total activity as 3 and 6 months of age in the U + U group. Latency in learning capacity was also noticed in this group. The results indicate that repeated exposures to ultrasound or its combination with X-rays could be detrimental to the embryonic development and can impair adult brain function when administered at certain stages of organogenesis.

From Ultrasound in Obstetrics: A Question of Safety <http://www.aimsusa.org/ultrasnd.htm>

Millions of women and their unborn children are being exposed to diagnostic ultrasound during pregnancy and childbirth without the women being advised prior to exposure that there has been no well-controlled scientific investigation carried out to study the delayed long-term effects of ultrasound on human development.Ova, embryos and fetuses are often exposed to prolonged sonography because the physician or technician lacks sufficient expertise to evaluate what he or she is seeing.

Recently the FDA yielded to pressure from industry and organized medicine to relinquish control over the amount of sonic energy that can be emitted by the new ultrasound devices used in obstetrics. The new ultrasound machines will beep at certain levels of energy output but essentially there will be little or no limit on the energy the health care provider may choose to use.

Despite the fact that the FDA's Center for Devices and Radiologic Health acknowledged the potential risks of ultrasound used in obstetrics in its 1982 publication "An Overview of

Ultrasound", edited by Stewart and Stratmeyer, there is no evidence that health care providers are obtaining women's truly informed consent to the use of ultrasound in pregnancy....

Numerous studies have been carried out to evaluate the effectiveness of routine diagnostic ultrasound. None has shown the routine use of diagnostic ultrasound to improve maternal and infant outcome over that achieved when diagnostic ultrasound was used only when medically indicated.

Are women overly concerned regarding the safety of ultrasound used in obstetrics? A letter published in the July 1988 issue of the British Journal of Obstetrics and Gynaecology, from Dr. Robert Bases, Chief of the Radiobiology Section, Albert Einstein College of Medicine, calls attention to the 1984 review by Stewart and Moore of over 700 publications since 1950 which demonstrate the present chaos in delineating and controlling exposure conditions and the bewildering range of ultrasound bioeffects. Bases states in his letter:

"The increased frequency of sister chromatid exchanges induced by pulsed ultrasound in human lymphocytes, first described by Liebeskind et al (1979), has been amply confirmed in reports from four independent laboratories involving studies of pulsed as well as continuous wave ultrasound (Haupt et al 1981; Ehlinger et al 1981; Ozawa et al 1984; Stella et al 1984). Recently further evidence that sister chromatid exchanges in human lymphocytes are induced by high-intensity pulsed ultrasound has been presented by Barnett et al (1988), who are now able to confirm the previous results."

"Free radical production in amniotic fluid and blood plasma by medical ultrasound, probably following gaseous cavitation, has been detected by Crum et al (1987). This provides a likely mechanism for the origin of the DNA damage. Because of these confirmations and a recent report by Ellisman et al (1987) that diagnostic levels of ultrasound may disrupt myelination in neonatal rats, the need for regulation, guidance, and properly controlled clinical studies is clear."

The implications of premature ovulation after ovarian ultrasonography, reported by Testart et al, are disturbing. If ultrasound can affect the adult ovary, what then is the effect of ultrasound on the ova of the female fetus?

Even if we begin today to carry out a well-controlled investigation into the delayed long-term effects of obstetric ultrasound it will be 20 or 30 years before we will know whether ultrasound will be the DES of the next generation.

From Screening Ultrasonography in Pregnancy
<http://cpmcnet.columbia.edu/texts/gcps/gcps0046.html>

Routine third-trimester ultrasound examination of the fetus is not recommended. There is insufficient evidence to recommend for or against routine ultrasound examination in the second trimester in low-risk pregnant women.

The most important potential benefit of ultrasound screening is reduced perinatal mortality. Among the seven trials that evaluated an ultrasound before 20 weeks (with or without additional late ultrasound), only the Helsinki trial and a meta-analysis heavily influenced by that trial's results were able to demonstrate a statistically significant benefit in lowering perinatal mortality. Two trials showed nonsignificant reductions in mortality while the remaining four trials and another meta-analysis showed no mortality benefit. In the Helsinki trial, the overall perinatal death rate was 4.6/1,000 deliveries (n =18) in screened women versus 9.0/1,000

deliveries (n = 34) in unscreened women. In the experimental group, 11 induced abortions were performed because of ultrasound findings and two babies died with major anomalies, compared to no abortions and 10 deaths with anomalies in the control group. There was no difference in perinatal mortality when the induced abortions resulting from ultrasound detection of congenital anomalies were included as deaths in the analysis. The meta-analysis that reported a significant mortality reduction included the four then-published trials that compared routine to selective ultrasound scanning and that reported number of pregnancies, deliveries, and perinatal deaths. It also evaluated the live birth rate, which takes into account induced abortions for malformations, and found it to be identical in the screened and control groups. The largest trial to date, the RADIUS trial randomized 151 low-risk pregnant women to routine ultrasound scans at 15-22 and 31-35 weeks of gestation or to usual care, which included ultrasounds performed for indications that developed after randomization. The risk of fetal or neonatal death was the same in the screened (0.6%, n = 52) and control (0.5%, n = 41) groups. Including induced abortions for fetal anomalies (9 vs. 5 in the routinely and selectively screened groups, respectively) did not affect these estimates.

While ultrasound before 20 weeks allows earlier detection of fetal structural malformations, it is not clear that this results in improved outcome. In the Helsinki trial, early detection led to an increased rate of elective abortions (2.7/1,000 screened women vs. 0/1,000 control women) and therefore to reduced perinatal deaths (see above).On the other hand, in the RADIUS trial,38 screening had no statistically significant effect on the rate of induced abortion (n = 9 or 1.2/1,000 screened women compared to n = 4 or 0.5/1,000 controls). Although early detection might theoretically improve survival for infants with fetal anomalies if they could be delivered at tertiary care centers capable of immediate medical and surgical intervention, no significant effects of early detection on overall perinatal mortality, or on survival rates among infants born with acute life-threatening anomalies or with any major anomalies, were seen in the RADIUS trial. Other trials of routine ultrasound before 20 weeks have detected too few (i.e., 0-2) malformations to allow meaningful comparisons of outcomes. None of the trials has evaluated whether routine screening improves outcomes in newborns with nonlethal anomalies.

A National Institutes of Health consensus development conference recommended that ultrasound imaging during pregnancy be performed only for a specific medical indication and not for routine screening. This is also the position of the American College of Obstetricians and Gynecologists. The Canadian Task Force on the Periodic Health Examination found fair evidence to recommend a single second-trimester ultrasound examination in women with normal pregnancies, but concluded that there was insufficient evidence to recommend the inclusion or exclusion of routine serial ultrasound screening for IUGR in normal pregnancies.