Attachment To:

"Big Drugs, Pregnancy and Social Marketing II"

By Norman E. Kjono

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The following six pages contain the full, unedited text of interview correspondence between Norman E. Kjono and University of Washington study author Lisa Gatzke-Kopp July 6-7, 2007

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——Original Message——
From: Norm Kjono [mailto:normkarl@earthlink.net]
Sent: Friday, July 06, 2007 10:02 AM
To: 'tbeaucha@u.washington.edu'
Cc: 'lisakopp@u.washington.edu'; 'bethr@u.washington.edu'
Subject: "Direct and Passive Prenatal Nicotine Exposure and the development of Externalizing Psychopathology"

Assoc. Professor Beauchaine and Ms. Gatzke-Kopp,

I am a Web site columnist who has written about tobacco control for the past several years. I have called both of you at the telephone numbers listed in the University of Washington Department of Psychology directory. Since you were not available when I called I left a message.

I read with interest the June 28, 2007 article in the Seattle Times concerning your recent study, **"Secondhand Smoke May Affect Brain of Fetus:"**

> "Pregnant women who are chronically exposed to secondhand smoke may have children who are at greater risk of problems related to attention and emotion, University of Washington researchers believe. In a study released Wednesday, scientists found that children who have such psychological problems have a higher frequency of them — or more severe troubles — if their mothers were regularly exposed to tobacco smoke while pregnant. Those troubles include Attention Deficit Hyperactivity Disorder (ADHD), aggressive behavior, defiance and a behavior pattern called conduct disorder, which can include truancy, fighting, failing in school, substance abuse, theft and property destruction. "Parents should be really aware of the [fetal] brain development going on during pregnancy," said psychologist Lisa Gatze-Kopp, lead investigator of the study, which was reported in the current issue of the journal Child Psychiatry and Human Development. . . . Mothers exposed to nicotine — the smoking mothers and the secondhand smoke mothers — generally had children with more severe problems with attention or more severe emotional and behavioral problems than the children of nonsmokers, said Gatze-Kopp. She said the findings could extend to all children whose mothers were exposed to tobacco smoke during pregnancy.

I will be doing a follow up to my recent column regarding your study, **"Direct and Passive Prenatal Nicotine Exposure and the Development of Externalizing Psychopathology"**. I would like to provide an opportunity for the study authors to comment or respond for publication prior to publishing that follow-up commentary. I would be interested in, and appreciate, your responses to the following questions:

1. You state in the study that "Secondhand smoke exposure was encoded as one because there was no reliable way to quantify exposure more specifically." The study text also states that "Self-reported smoking categories were weighted by severity by coding occasional smoking as one . . ."

> a.) Does this coding system as used in your calculations attribute firsthand smoking consequences to Environmental Tobacco Smoke (ETS) exposure?
>
> b.) How did you account or adjust for the fact that if there was "no reliable way to quantify exposure more specifically" then the magnitude of ETS exposure was unknown?

2. Both the Seattle Times June 28, 2007 article and the text of your study attribute the observed pathological child behavior effects to nicotine.

> a.) Do you contend or assume that nicotine ingested through exposure to ETS is of the same magnitude and physiological impact as that attributed to firsthand smoking?
>
> b.) Did you include any controls for the possibility that study participants may have used pharmaceutical Nicotine Replacement Therapy (NRT) delivery device products?

3. Many of the child behavior problems that you report as being associated with nicotine through exposure to ETS are also associated with pregnant mothers' use of antidepressant medications.

a.) Do you contend or assume that nicotine is the causal factor for all observed child behavior pathology that you report?

b.) Did you include any controls for the possibility that study participants may have used pharmaceutical Nicotine Replacement Therapy (NRT) delivery device products?

4. Many child behavior problems are also attributed to parental stress and lower social-economic status. Statistically, persons who smoke tend to be heavily weighted toward lower economic status. The child behavior problems in that category include those which you associate with exposure to nicotine.

a.) Do you contend or assume that exposure to nicotine in ETS is a more powerful predictor of child behavioral problems than parental stress and/or lower socio-economic status?

b.) Did you include any controls for the confounding variable that observed child behavior may be causally associated with socio-economic status and not caused by exposure to ETS?

5. Do you contend that there is a causal relationship – versus an observed association — between pregnant mothers' exposure to ETS and child behavior pathology?

Thank you for your attention to these matters. I appreciate that you took the time to consider the above questions. I look forward to your response.

Sincerely,

Norman E. Kjono
(425) 497-8187

——Original Message——
From: Lisa Kopp [mailto:lisakopp@u.washington.edu]
Sent: Friday, July 06, 2007 1:01 PM
To: Norm Kjono
Subject: Re: "Direct and Passive Prenatal Nicotine Exposure and the development of Externalizing Psychopathology"

Dear Norm,

I am sorry I missed your call this morning. I have inserted answers to your questions below. Feel free to email me if you have any further questions.

At 10:01 AM 7/6/2007 -0700, you wrote:

Assoc. Professor Beauchaine and Ms. Gatzke-Kopp,

I am a Web site columnist who has written about tobacco control for the past several years. I have called both of you at the telephone numbers listed in the University of Washington Department of Psychology directory. Since you were not available when I called I left a message.

I read with interest the June 28, 2007 article in the Seattle Times concerning your recent study, **Secondhand Smoke May Affect Brain of Fetus:**

Pregnant women who are chronically exposed to secondhand smoke may have children who are at greater risk of problems related to attention and emotion, University of Washington researchers believe. In a study released Wednesday, scientists found that children who have such psychological problems have a higher frequency of them — or more severe troubles — if their mothers were regularly exposed to tobacco smoke while pregnant. Those troubles include Attention Deficit Hyperactivity Disorder (ADHD), aggressive behavior, defiance and a behavior pattern called conduct disorder, which can include truancy, fighting, failing in school, substance abuse, theft and property destruction. "Parents should be really aware of the [fetal] brain development going on during pregnancy," said psychologist Lisa Gatze-Kopp, lead investigator of the study, which was reported in the current issue of the journal Child Psychiatry and Human Development. . . . Mothers exposed to nicotine — the smoking mothers and the secondhand smoke mothers — generally had children with more severe problems with attention or more severe emotional and behavioral problems than the children of nonsmokers, said Gatze-Kopp. She said the findings could extend to all children whose mothers were exposed to tobacco smoke during pregnancy.

I will be doing a follow up to my recent column regarding your study, **Direct and Passive Prenatal Nicotine Exposure and the Development of Externalizing Psychopathology**. I would like to provide an opportunity for the study authors to comment or respond for publication prior to publishing that follow-up commentary. I would be interested in, and appreciate, your responses to the following questions:

1. You state in the study that Secondhand smoke exposure was encoded as one because there was no reliable way to quantify exposure more specifically.The study text also states that Self-reported smoking categories were weighted by severity by coding occasional smoking as one . . .

a.) Does this coding system as used in your calculations attribute firsthand smoking consequences to Environmental Tobacco Smoke (ETS) exposure?

This coding system was not designed to make statements about the equivalence of occasional direct smoking and chronic smoke exposure. The only reliable quantification scheme would be to assay metabolite levels in blood or urine, ideally of the fetus but of the mother as well. Our coding system was designed not to overestimate the enviornmental smoke exposure, while at the same time allowing it to contribute to a total exposure score. However, I call your attention to a recent report by the Surgeon General on second hand smoke exposure. Several studies have found that individuals who are merely exposed second hand, can show blood levels that would classify them as smokers. So chronic, indoor, exposure can certainly accumulate in the bloodstream of an individual who is not actively smoking.

b.) How did you account or adjust for the fact that if there was no reliable way to quantify exposure more specificallythen the magnitude of ETS exposure was unknown?

We focused only on women who had regular exposure in the 2nd or 3rd trimester (when the developing brain is most vulnerable) in the home or at work. This was meant to capture women who were around individuals who were smoking every day, and indoors. This is not meant to address the risks of occasional, infrequent, or mild exposure such as eating in a restaurant where smoking takes place, or visiting a relatives house for a weekend. This is meant to address the risks of long term, high level exposure, such as a waitress might experience in a bar or restaurant where smoking is permitted.

2. Both the Seattle Times June 28, 2007 article and the text of your study attribute the observed pathological child behavior effects to nicotine.

a.) Do you contend or assume that nicotine ingested through exposure to ETS is of the same magnitude and physiological impact as that attributed to firsthand smoking?

Our contention that nicotine is a mechanism by which changes occur in the central nervous system during development follows from extensive research conducted in animals where experiments are capable of isolating the effects of nicotine from other teratogens present in tabacco smoke (such as tar) and from hypoxia, or oxygen restriction to the fetus, that also occurs when a mother smokes. Our interest in nicotine exposure stems from the fact that that changes that nicotine can make to the brain during development affect the same systems that are of interest to researchers interested in behavior disorders. This is in contrast to emotional disorders, such as depression, which result from changes in other brain regions, and which appear unaffected by exposure to nicotine.

We do not contend that second hand exposure and direct exposure are necessarily equivalent. However, it is possible for individuals exposed on a regular basis to second hand smoke to show blood levels of nicotine metabolites that would identify them as a smoker. It was this level of exposure we were hoping to achieve by studying only women with regular exposure in the home or at work, and not occasional exposure. However, because we were studying women after the pregnancy, we could not quantify the exposure through blood or urine testing— as would be ideal.

b.) Did you include any controls for the possibility that study participants may have used pharmaceutical Nicotine Replacement Therapy (NRT) delivery device products?

Generally the blood concentration of such products is well below that of smoke inhalation because the body has the opportunity to significantly metabolize the nicotine before it is widely circulated (unlike when a substance is inhaled). We also eliminated women who quit early in pregnancy— who may have been more likely to use such products. Only women who verified that they did not smoke during any trimester of pregnancy were included in the second hand exposure group. We did not separately code for the additional use of nicotine patches, or their replacement use in the event that they had quit prior to the pregnancy.

3. Many of the child behavior problems that you report as being associated with nicotine through exposure to ETS are also associated with pregnant mothersuse of antidepressant medications.

a.) Do you contend or assume that nicotine is the causal factor for all observed child behavior pathology that you report?

We are absolutely not trying to say that all behavior problems resulted from the exposure to the smoke. In fact, all children in the sample had behavior and/or emotional difficulties. However, the smoke exposure— direct or second hand— was associated specifically with increased severity of ADHD and/or conduct disorder, and not other types of childhood psychopathologies. This is consistent with the literature both on what brain regions are associated with these types of behavioral difficulties, and how nicotine works in the developing brain. Other factors undeniably

contribute to child behavioral pathology, we are simply trying to illustrate that nicotine makes an additional, and independent, contribution to the vulnerability for these disorders.

b.) Did you include any controls for the possibility that study participants may have used pharmaceutical Nicotine Replacement Therapy (NRT) delivery device products?

This is answered above.

4. Many child behavior problems are also attributed to parental stress and lower social-economic status. Statistically, persons who smoke tend to be heavily weighted toward lower economic status. The child behavior problems in that category include those which you associate with exposure to nicotine.

a.) Do you contend or assume that exposure to nicotine in ETS is a more powerful predictor of child behavioral problems than parental stress and/or lower socio-economic status?

What we can say is that the association between smoking behavior and lower SES is somewhat culturally specific, and more recent. As more and more information becomes available of the dangers, higher education and resources are associated with the choice not to smoke. However, prior to this information being available, and in other countries where the ability to afford smoking is a status symbol, this association does not hold. Many other studies have identified an association between direct maternal smoking and antisocial behavioral outcomes in the offspring both in older cohorts (mother's smoked before any information about the dangers were available) and in other countries.

In addition, the sample studied in our paper equalized some of these effects across the three groups (non-smoked exposed, smokers, and second hand exposed). In fact, the mothers with second hand exposure had the same education levels as the non-smoking mothers (although the smoking mothers did show lower education levels). Although we absolutely agree that such social and environmental factors contribute to child well being (or can detract from it) these variables often affect child psychopathology in a general way. Our findings were specific to a specific form or type of psychopathology, again, consistent with the theorized brain mechanisms involved. In addition, our analyses demonstrate the smoke exposure contributed independently to externalizing behavior problems even after social factors were controlled for statistically.

b.) Did you include any controls for the confounding variable that observed child behavior may be causally associated with socio-economic status and not caused by exposure to ETS?

I am not entirely sure I understand what you are getting at, but I think I may have addressed it above. If not, let me know.

5. Do you contend that there is a causal relationship versus an observed association — between pregnant mothersexposure to ETS and child behavior pathology?

What we are suggesting is that when exposure is chronic, the nicotine absorbed into the mother's blood passes to her fetus and affects brain development. This is supported by the findings that the developing brain is supremely sensitive to nicotine and is affected at doses lower than those required to affect physical growth. We often associate smoking with a risk for "low birth weight", but the brain is affected at lower doses than those required to reduce birth weight. The Surgeon General released a report last year documenting the extensive dangers of second hand smoke exposure— including those to the fetus of an exposed mother. Our study aimed to extend the documentation of risks into psychological well being as well as physical health. Our study in unable to draw conclusions about causality, a consequence of doing research with humans instead of animals. But a large body of research gives us good reason to suspect a direct link, and to take appropriate measures both personally, and through public policy, to protect women and their babies from potential harm.

Thank you for your attention to these matters. I appreciate that you took the time to consider the above questions. I look forward to your response.

Sincerely,

Norman E. Kjono

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