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EVIDENCE FOR METHYL NITRITE AS AN EXHAUST COMPONENT FROM ENGINES WITH CERTAIN FUELS

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Abstract: In some areas of the United States (US), asthma prevalence has reached historically unprecedented highs. Three peer-reviewed studies in New York City found prevalence rates among children from 25% to 39%. That is not true in all places. For example, prevalence in Miami, Florida , was estimated to be only 6-10%. A recent study in major cities in Georgia found only 8.5%. One study in California found asthma prevalence was unrelated to local concentrations of criterion pollutants. In the US, all criterion pollutants, including PM2.5, show a downward trend over the last two decades. These facts argue against any significant influence of criterion pollutants in this crisis.These facts suggest that an unrecognized ambient pollutant may be the cause. One important study in southern California in mid-summer measured pulmonary function in children as it was related to outdoor ozone pollution. They found a negative association; higher levels of ozone were associated with improved respiratory function. We call this a "Paradoxical Ozone Association" (POA). Further evidence for a POA appears in seven other studies in Los Angeles, London, Scotland, and southeastern Canada.One plausible explanation for these observations would be the production of methyl nitrite (MN) as an exhaust product of MTBE in gasoline. Unlike ozone, MN is rapidly destroyed by sunlight. All of the POA studies were done in regions with significant methyl ether in gasoline. This explanation is strengthened by the observation that a POA has not been seen in regions without ether in gasoline.A previous AWMA paper proposed a plausible chemical model predicting that MTBE in gasoline will create MN in the exhaust. MN is highly toxic and closely related alkyl nitrites are known to induce respiratory sensitivity in humans. Funding to measure MN has not been available.

Keywords: asthma, biodiesel, diesel, DME, Japan, MTBE, exhaust, ozone, nitrite, NOy, sensitivity

INTRODUCTION

The basic premise of this paper is that methyl nitrite (MN or MeONO) is a very important component in the exhaust of engines with methyl ether (such as MTBE or DME) in the fuel, and that past exhaust speciation studies have overlooked this possibility. While the available data do not prove that this is true, we shall show that existing data and research are entirely compatible with the idea. Essentially, this paper will present various kinds of evidence that the idea may be true, so that further research is warranted.

The evidence presented will be of three kinds: (1) an understanding of the chemistry of methyl ether in engine exhaust, (2) the known toxicology of other alkyl nitrites similar to MN, and (3) various kinds of epidemiologic evidence that strongly support the idea.

The strongest evidence comes from various epidemiologic studies whose results are inexplicable in terms of current understanding of ambient air pollution.

The most important such evidence is the observation of negative ozone-health associations seen in several studies in several parts of the world. All of those studies were done in regions with substantial amounts of methyl ether in gasoline. We propose that the negative associations can be easily explained by the fact that sunlight is known to photolyse (Goss, et al. 2004) MN, with a half-life of about 10-15 minutes in direct sunlight (Seinfeld et al. 1998). That is due to the presence of strong ultraviolet absorption bands in the wavelength range 360nm to 380nm. Sunlight at the earth's surface has strong components in that wavelength range. Since sunlight is necessary to create ozone by photo-oxidation, sunlight will have opposing effects on ozone and MN, so that the two pollutants will be negatively correlated. That is, in any given geographic location, the days with the least ozone will be the days with the most MN.

It is known (Jonsson et al. 1982) that gasoline without ether does not create MN in the exhaust. Hence there was essentially no MN from American gasoline prior to the introduction of MTBE in 1979. MTBE was initially used only to raise the octane of premium grades of gasoline. However, in the US in the mid-1990s, the usage was greatly increased for use as a mandatory oxygenate in all gasoline, but only in certain geographic regions.

Some additional support comes from three epidemiologic studies that linked, with very high statistical significance, mandatory MTBE in gasoline to various symptoms, including those of asthma and allergic rhinitis. In addition, we note that truly unprecedented prevalence rates for asthma have been seen in several American cites with such mandatory MTBE, but not in other cities without it. The timing of the increases in asthma prevalence is consistent with the known historical timing of the introduction of oxygenated or reformulated (RFG) gasoline with MTBE used as the oxygenate.

THE CHEMICAL MODEL FOR EXHAUST FROM METHYL ETHER

Before explaining the model that predicts MN in MTBE exhaust, we should ask what previous exhaust speciation studies have shown. Most of those studies were not equipped to identify MN if it was present, and none describe any attempts to look for it. However, many such studies do show several percent "unidentified compounds" (Hoekman et al., 1992; Kirchstetter et al., 1999). Hence it is entirely possible that MN in engine exhaust has been overlooked. A previous AWMA paper (Joseph, 1999) presented a model (available on-line at http://www.osti.gov/em52/eprints/99885.pdf) that predicts MN in exhaust from engines with MTBE in the fuel. We can summarize this model in four steps:

(1) Some MTBE in gasoline escapes combustion and appears in the exhaust. This is a proven fact (Hoekman et al., 1992).

(2) Nitric oxide (NO) is an important component in engine exhaust. This is a proven fact (Heywood, 1988).

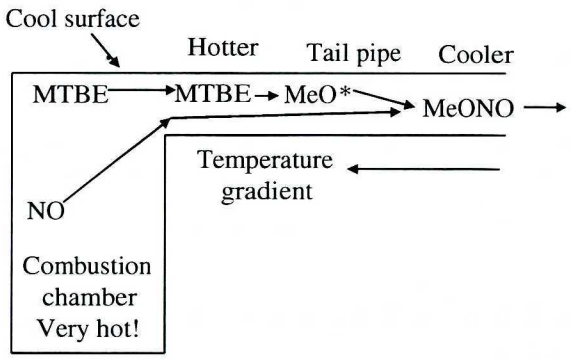
(3) Some MTBE in the exhaust pipe pyrolyzes into methoxy (CH_3O) and tert-butyl (C_4H_9) radicals. A previous paper (Joseph, 1999) analyzed data supporting this reaction. The reaction was also identified in an early laboratory study (Brocard, et al., 1983) of MTBE oxidation at low temperatures, as well as in a more recent modeling study (Bohm, et al., 2000).

(4) The NO in the exhaust pipe can serve as a trap for methoxy radicals and thus form MN (CH_3ONO). This is a proven fact, as has been observed in several laboratory studies (Batt, 1979; Batt, L, 1987; Wallington, et al. 2003)

A key concept in this model is that the relevant chemistry takes place in the exhaust pipe, not in the main combustion chambers of the engine. The reason is that, while methoxy radicals are known to be intermediate states in fuel combustion, the temperatures in the combustion chambers are so high (> 2000° K) that the methoxy radicals are almost immediately pyrolyzed. However, as was shown in the previous paper (Joseph, 1999), it is likely that the methoxy radicals formed in the exhaust pipe will survive long enough to form MN, and that the MN so formed will most likely survive into the ambient air. Indeed, we expect that the longitudinal temperature gradient in the exhaust pipe will facilitate this survival. These ideas are illustrated in figure 1.

Caption to figure 1: Schematic diagram of the relative roles of the main combustion chamber of the engine and the exhaust pipe. For ethers, important chemistry, including pyrolysis and subsequent free-radical associations, can take place in the exhaust pipe because its temperature is lower than that of the main combustion chamber. In the absence of sunlight, MN is stable in air (Goss, et al., 2004).

Figure 1: The exhaust pipe is critical



Low concentrations of MN have been seen in the exhaust of a diesel engine with methanol in the fuel (Jonsson, et al, 1982). This can be taken as proof that it is possible to produce MN in vehicle exhaust. However, alcohols are much less likely than ethers to pyrolyze into methoxy radicals, as in step #3 of the above model, so we do not expect that the use of ethanol as oxygenate will have the same harmful effects that we attribute to MTBE. This distinction between the effects of ethanol and MTBE is also supported by various anecdotal reports of people who were severely affected from MTBE in gasoline but not from ethanol (Joseph, et al. 2002).

There is considerable literature suggesting that MeONO is produced as a combustion product of methanol. However, there are convincing data that those measurements were artifactual, due to methanol in the exhaust sample reacting with NO_2 to form the MeONO (Finlayson-Pitts, et al.,1982). This is especially likely if the exhaust products are stored in a bag for a period of several hours.

However, the absence of MN in the exhaust of methanol does not imply that methyl ether will not produce MN. We are concerned that efforts to reduce particulate pollution by adding di-methyl ether (DME) to diesel fuel may also produce MN. Pyrolysis of DME (Batt, 1982) definitely produces methoxy radicals as in step 3 of the above model. We are especially concerned that Japan (Kajitani, et al., 2003) has already begun major investments in plants to manufacture DME to use in diesel fuel.

CHEMICAL EVIDENCE FROM THE UTAH EFFECT

A group under the direction of Delbert Eatough (Du, 1997) has reported measurements of the ratio of SO_4 (sulfate particles) to SO_2 (gas phase) in Utah County, Utah, during two winters when oxygenated gasoline (WOG) was used. During the winter of 95-96, they found that the sulfate/SO_2 ratio roughly doubled during the period of WOG. At that time, 28% of the oxygenate used was MTBE. The increase in SO_4 was unusual in that it occurred only during nighttime hours, in contradistinction to the better understood photo-oxidation process that occurs during daylight. The obvious implication was that some oxidizing agent was being directly or indirectly produced by oxygenate combustion.

However, when the experiment was repeated during February 1997, no increase in sulfate was observed. (D. Eatough, 1998, private communication) During that time, only ethanol was used as the oxygenate.

We suggest that MN in MTBE exhaust may explain these observations. The main point is that MN, under some circumstances, is known to catalyze oxidation. In vivo, it is known to (permanently) oxidize hemoglobin in red blood cells to methemoglobin (Wax, 1994). More relevant here are some early laboratory studies in Russia (Gimmelman, et al. 1937) showing that MN will catalyze the oxidation of some hydrocarbon fuels in the gas phase. Hence, this effect could explain both the nocturnal observation of increased SO_4/SO_2 ratio in Utah in 1996, as well as the failure to observe the increase in 1997.

The Utah group hypothesized that their result was due to aldehyde production from the oxygenates, but provided no concurrent measurements of aldehyde concentrations. However, formaldehyde is not easily photolyzed by sunlight, and in fact is larger in summer than in winter. Thus formaldehyde does not explain the Utah effect as well as MN does.

THE IMPORTANT TOXICOLOGY OF METHYL AND OTHER ALKYL NITRITES

First, we point out that our thesis concerns the health effects of methyl nitrite, not MTBE. Hence most previous studies of the toxicology of MTBE are irrelevant. For example, the State of Wisconsin, prompted by literally thousands of Milwaukee residents who believed that MTBE in gasoline was sickening them in early 1995, conducted an emergency study. They found that people's symptoms were

not related to whether consumers purchased gasoline oxygenated with MTBE as compared with ethanol. But when driving in city traffic you breathe the exhaust of those vehicles in front of you, not your own, so the type of gasoline you purchased is irrelevant. Thus, the Wisconsin study in no way disproves our thesis. Another paper (Joseph et al. 2002) analyzed several other early studies of MTBE that (incorrectly, we believe) concluded that MTBE in gasoline has no harmful effects.

Methyl nitrite (MN) is one of a class of compounds called alkyl nitrites, with the generalized formula R-O-N=O. MN is the simplest and lightest compound in this class. The lethal concentration of MN by inhalation in a four hour exposure to rats is only 170 ppm (Klonne et al., 1987). This is 100 times less than the corresponding value for benzene, for example, and 12 times less than carbon monoxide. A review is available on-line at http://www.osti.gov/em52/eprints/methylnitrite.pdf.

There have been several reports (Slovak et al., 1981) of accidental exposure of industrial workers to MN, resulting in methemoglobinemia sufficiently serious to require immediate hospitalization. Prominent symptoms include headache and heart palpitations (Wax et al., 1994; Adams, 1964). These symptoms are both very significant for our purpose, since headache was the most common complaint found by the CDC investigations of health problems from MTBE in both Alaska (Moolenaar et al., 1994) and Connecticut (White et al. 1995). Furthermore, statistical data from the Philadelphia Department of Health (Joseph, 1999) indicate that the number of people treated for cardiac dysrhythmia increased very substantially between 1993 and 1996, the first three years of large scale MTBE usage in that city.

What is relevant here is chronic exposure to low concentrations. On that there is far more information available on the higher alkyl nitrites, amyl and n–butyl nitrite, since these are established as drugs of abuse due to their neurological effects. (The US National Academy of Sciences has classified MN as a "neurotoxicant".
See http://www.nap.edu/books/0309045312/html/10.html#p200066719960010001). An older review (Haverkos et al., 1988) (also available on-line at http://www.drugabuse.gov/pdf/monographs/83.pdf) cites many studies showing that chronic exposure to alkyl nitrites can diminish immune function, inducing allergy and chemical sensitivity

Amyl nitrite can induce respiratory symptoms in humans, including tracheobronchitis, cough, and dyspnea (Haverkos et al., 1988). However, alkyl nitrites are not classical respiratory irritants. Indeed, they are commonly used as diagnostic agents in adults (Nakatani et al., 1996) and even therapeutically in infants (Moya et al., 2002). Hence the respiratory effects are probably due to sensitivity acquired from multiple exposures. Humans can develop allergic reactions to organic nitrites (Dax et al., 1989).

Finally, MN has been shown to be mutagenic by the Ames test (Tornqvist et al. 1983). This implies, with a probability of about 90%, that it is carcinogenic.

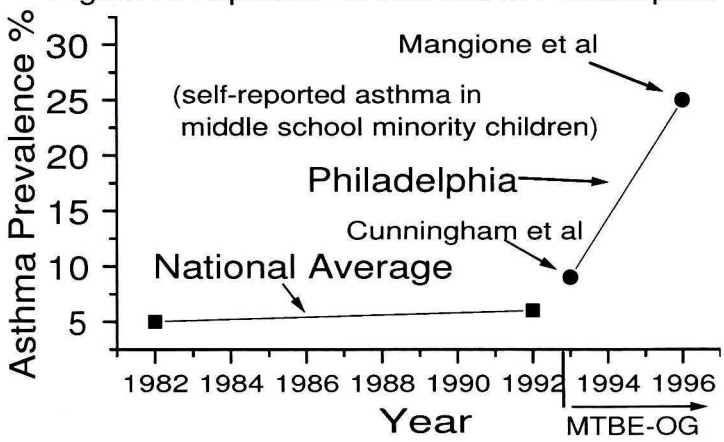
DATA LINKING ASTHMA TO MTBE

A previously published editorial (Joseph, 200) noted that there were preliminary reports of very large and rapid increases in asthma prevalence in regions of the United States with MTBE-RFG but not in other regions without it. More-recent studies support that observation.

A study (Webber et al. 2002) in New York City indicated asthma prevalence in the range 20-32%. Another study (Nicholas et al., 2005) found that 25% of the children in Harlem (New York City) had asthma; the title of that paper contains the phrase "Asthma Crisis". A study (McLean et al., 2004) of homeless children in New York City found asthma prevalence to be 39.8%. We suggest that homeless children spend more nights at street level and so are more exposed to vehicle exhaust than are those living in tall apartment buildings (which are very common in NY City).

By contrast, studies of asthma prevalence in regions of the US without mandatory MTBE in gasoline do not show such high levels. A study (Brito et al. 2000) in Miami, Florida estimated prevalence of only 6-10%. Another example is a CDC study in Georgia (Mellinger-Birdsong et al., 2003) that showed asthma prevalence of only 8.4% in the major cities in that state. Until January 2004 New York City had MTBE-RFG, while Florida and Georgia have never had it. We know of no US study demonstrating asthma prevalence greater than 10% in regions without mandatory MTBE in gasoline. A more systematic study of these geographical associations is needed.

Figure 2: Explosion of Asthma in Philadelphia



Two different studies in Philadelphia illustrate the magnitude of the problem (Fig 2).

We know of no other plausible explanation for these historical and geographical associations of asthma prevalence with the usage of MTBE in gasoline.

EXPLAINING THE PARADOXICAL OZONE ASSOCIATIONS

Perhaps the strongest evidence for MN as an important ambient pollutant comes from several peer-reviewed studies of the influence of ambient ozone on human health (mainly, but not exclusively, asthma in children). Seven studies, all in regions with methyl ether in gasoline, found negative associations, i.e., a negative coefficient for morbidity versus ozone concentration using linear regression analysis. In every case, the authors themselves indicated that this aspect of their data was unexpected and inexplicable.

As we have explained, ambient MN will be large when ozone is low, and vice versa. Thus MN is a very plausible explanation for these paradoxical observations. Another paper examining those studies in more detail is currently in preparation. Here we will only summarize some of the more dramatic findings.

A remarkable result was seen in a study by Avol et al. (1998) of respiratory function in children in southern California during the spring and summer of 1994. The abstract states: "Wheezy children had the most trouble breathing during the summer on low-O_3 days" (emphasis added). The authors stated: "Some indices of lung function unexpectedly showed apparent improvement during periods of high ozone". Respiratory function was measured at both the beginning and end of the day. The influence of outdoor air pollution was evaluated by the difference between the evening and morning values; i.e., a negative difference represented a decline in respiratory function. This is one of the few studies that quite rigorously focused on the effects of ambient ozone, as opposed to various possible in-door pollutants. From these results we can infer that the effect of MN was worse than the highest levels of ozone seen in southern California in mid-summer!

Two pairs of studies in London, England, found POAs with high statistical significance. A group let by Hajat found POAs in two studies for respiratory symptoms in both adults and children (Hajat et al., 2002; Hajat, et al., 1999). Another pair of studies by Buchdahl is also noteworthy; both found a so-called "U-shaped" curve for the dependence on ozone concentration, i.e., an increase in morbidity as ozone concentrations dropped below 20 ppm, as shown in figure 3.

Figure 3: Taken with permission from Buchdahl et. al. (1996). The graphs show the associations of ozone, SO_2, and NO_2 with wheezing in asthmatic children. The U-shaped association with ozone is clear from the trend using Poisson regression (solid curve). There is no U-shape associated with SO_2 or NO_2, indicating that the effect is unique to ozone and is not the result of non-specific increase in various pollutants on days with "good" air quality (as defined by criterion pollutants).

The first Buchdahl study covered the period 1 March 1992 to 28 February 1993 while the second covered the period 1 December 1995 to 30 November 1996. In the later study an attempt was made to identify the cause of the U-shaped phenomenon; the researchers measured ambient concentrations of a wide variety of hydrocarbons in addition to the traditional "criterion" pollutants. They concluded: "Certain hydrocarbon pollutants accumulate in the atmosphere when ozone concentrations are low. However, the U-shaped association of ozone on incidences of wheeze cannot be explained by these other pollutants". However, those researchers did not measure ambient concentrations of MN.

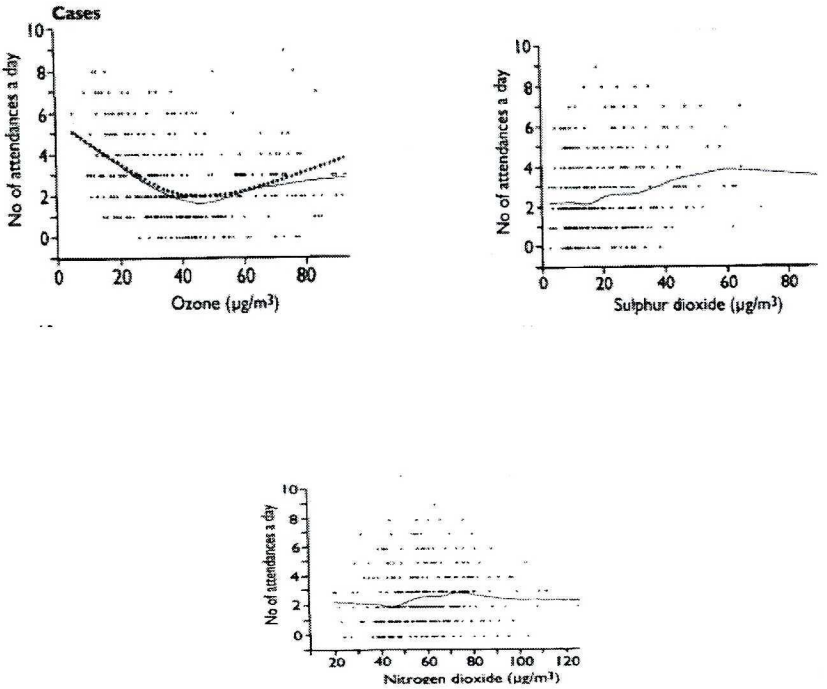


Fig. 3. The associations of ozone, SO_2, and NO_2 with wheezing in asthmatic children.

DISCUSSION

Here we will discuss various ways in which the apparent health effects of MN differ from those of more studied pollutants, especially ozone, free radicals, and various respiratory irritants such as the strong acids.

As we mentioned, MN is not a classical respiratory irritant. That is, it does not immediately create respiratory or irritant symptoms upon exposure to most people. Rather, there is evidence (Haverkos et al. 1988) that chronic exposure to alkyl nitrites can gradually alter the immune and neurological systems so as to create excessive sensitivity to future exposures. This situation is very similar to the well studied phenomenon of occupational asthma from chronic exposure to very low levels of toluene di-isocyanate (TDI) (Mapp, et al. 1988). Initially, most workers are not affected by exposure to TDI. However, with the passage of a few years of chronic exposure, more and more workers will develop rather severe asthma, i.e., asthma attacks occur immediately upon future re-exposure to TDI.

Evidence for this slowly developing (MTBE-related) sensitivity is most clearly demonstrated in the study (Joseph et al. 2002) of visits to physicians in Philadelphia between 1992 and 1997. (Gasoline was oxygenated with MTBE in the winters starting in 1992-93, and then all year starting in January 1995.) All of the symptoms which showed increases did so in a gradual growth over the six years of the study. This occurred, for example, for wheezing (505 % increase), cough (220%), allergic rhinitis (114%), skin rash(625%), and "general allergy" (395%). Most unusual was a large increase in adult-onset asthma - a disease that does not normally arise in the absence of significant toxic or allergenic exposure.

MN is only slightly soluble in water, but is soluble in fat. This implies that the physiological mechanism of induced pathology is probably very different from that of the more water-soluble pollutants, such as ozone, aldehydes, and strong acids. Indeed, many of the so-called "irritant receptors" in the lung are actually lipophilic (Nielsen, 1991), and their excitation leads to neurological impulses to the lungs, eyes, brain, and other organs. An excellent review on this subject is the paper by Shusterman (2002). Figure 2 in the Shusterman paper shows the different organs which are attacked by sulfur dioxide, ozone, and hydrophobic pollutants, respectively. According to Shusterman, what most people would consider a "pure odor" (including perfumes) can elicit asthma and/or panic attacks in sensitive people.

Finally, we want to point out that ethers are not the only possible source of MN in engine exhaust. In particular, we are very concerned that increasing use of so-called "biodiesel" may also be an important source of ambient MN. "Biodiesel" means methyl esters of organic fatty acids. These esters may be expected to pyrolyze into methoxy radicals, leading to the production of MN by the same mechanism as the ethers. Since use of biodeisel is growing rapidly, we emphasize the urgency of determining if biodiesel use does produce MN in the exhaust.

CONCLUSIONS

In summary, there is considerable evidence that MN may be an important exhaust product of methyl ethers in gasoline, and that it may be responsible for the worst epidemic of asthma in human history. This possibility was first presented in an editorial (Joseph, 200). After discussing future research needs, the last sentence in that editorial said: "It is imperative that funding agencies recognize the importance of this research." To date, that message has fallen on deaf ears.

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