American Journal of Medical Case Reports, 2014, Vol. 2, No. 11, 232-236
Available online at http://pubs.sciepub.com/ajmcr/2/11/2

DOI:10.12691/ajmcr-2-11-2

Rhabdomyolysis Complicating Acute CO Poisoning: A Case Study and a Review

Shimaa M. Motawei[1,*], Salwa M. El-Wasify[2], Sahar A. Eldakroury[1], Adel M. Elmansoury[1]

[1]Forensic Medicine & Clinical Toxicology, Mansoura University Emergency Hospital, Mansoura, Egypt
[2]Nephrology Department, Urology & Nephrology Center, Mansoura University, Egypt
*Corresponding author: sh-mm@mans.edu.eg, shimaa_motawei@yahoo.com

Received October 17, 2014; Revised October 25, 2014; Accepted October 28, 2014

Abstract **Introduction:** Carbon Monoxide (CO) is a colourless, odourless, tasteless gas. Mild poisoning by CO can be Mistaken for a non-specific headache or a viral illness headache or viral illness. Moderate to severe CO poisoning produces significant morbidity and mortality that provokes treatment controversy. Rhabdomyolysis, compartment syndrome, renal failure and peripheral neuropathy are unusual complications of CO That can be faced during practice and should be considered by physicians. **Case presentation:** A 34-years old Egyptian male was referred to the Toxicology Unit from the ED for evaluation of his lower limb weakness. Initial examination revealed a fully conscious patient with stable vital signs and arterial blood gases. However, the patient cannot stand steadily or walk. Neurologic examination revealed hypotonia and diminished reflexes in both lower limbs. No history of toxin exposure but a condition of sudden acute illness affecting him and his parents and upon which his old-age parents, were transferred to ICUin coma. Investigations revealed increased serum alanine transaminase and serum creatinine. A work-up that involved appropriate imaging and serum creatinekinase (CK) measurement revealed extremely elevated serum CK, normal appearance of liver and increased echogenicity of both kidneys with preserved cortico-medullary differentiation. Based on the above-mentioned data, a diagnosis of rhabdomyolysis complicating acute CO exposure with secondary renal insult was made. The patient begins haemodialysis with follow up of his serum K^+, creatinine and CK. After one month, levels of serum creatinine and alanine transaminase became normal. The patient underwent rehabilitation therapy to improve his neuromuscular state. **Conclusion:** Carbon monoxide poisoning should be suspected in patients presented with acute illness without prior medical or surgical cause, and rare complications of CO poisoning like rhabdomyolysis should be suspected particularly in patients with delayed seek of medical care. Timely prompt medical care involving team therapy is necessary to prevent further complications like RF and muscle wasting.

Keywords: *acute CO poisoning, complications, rhabdomyolysis, acute renal failure*

Cite This Article: Shimaa M. Motawei, Salwa M. El-Wasify, Sahar A. Eldakroury, and Adel M. Elmansoury, "Rhabdomyolysis Complicating Acute CO Poisoning: A Case Study and a Review." *American Journal of Medical Case Reports*, vol. 2, no. 11 (2014): 232-236. doi: 10.12691/ajmcr-2-11-2.

1. Introduction

Carbon monoxide is a colourless, odourless, non-irritating gas that has almost the same density as air, so distributes equally throughout an enclosed area. CO penetrates through standard drywall and separate units of a multifamily dwelling, being a small non-polar molecule [1]. Reviewing the literature revealed that headache, dizziness, dyspnea, coma, hypotension and syncope are the main presenting features of CO poisoning, and that rhabdomyolysis, renal failure and peripheral neuropathy are rare complications of CO poisoning [2]. Here, a case of rhabdomyolysis and acute renal failure complicating CO poisoning will be discussed.

2. Case Presentation

A 34-years old non-smoker Egyptian male who is married and has two offspring and is working in mechanics repair, came to the Emergency Department of Mansoura University Hospital on Tuesday 15th January 2013; seeking the medical care for his inability to walk or stand steadily. The condition started since one day after sharing a meal of fish and then his parents were found at home by the neighbours in a bad condition and were transferred to the nearest hospital.

The patient received fluids therapy and O_2 inhalation and felt better while his parents were in coma and suffering from respiratory depression and are still hospitalized in ICU on mechanical ventilation, as given by history. The provisional diagnosis made by the referring physician was 'Food Poisoning'. The patient was referred to the Toxicology Unit at Mansoura University Emergency Hospital. On examination, the patient was fully conscious with stable vital signs. His BP was 120/80 mmHg, pulse 85/min. regular, full; RR 20 breath/min., rectal temperature 37°C. Pupils were rounded, regular, reactive, equal and central. Chest examination revealed

bilateral vesicular breath sounds and clear chest. Finger stick bedside blood glucose was 86 mg/dl. ECG revealed normal sinus rhythm without ischaemic changes. Arterial blood gas (ABG) results showed PH 7.36, PCO_2 35 mmHg, PO_2 99 mmHg, $HCO_3$24 mEq/L.

Neurologic examination revealed hypotonia and impaired reflexes in both lower limbs, sparing the upper limbs. The patient denied flu symptoms in the previous days (This excludes infectious causes of acute muscle weakness as Guillan-Barre syndrome) or a family history of muscle dystrophies or neurologic diseases (This excludes familial muscle dystrophies as a cause of hypotonia).Carboxyhaemoglobin level was investigated and found to be 1.8% (Normal range is 1-2 % in non-smokers). Other abnormal haemoglobin forms were investigated also and showed Meth Hb 1.8 (Normal range 0.1-1%) and SulfHb 2.2% (Normal range 0.5 – 1.5 %) [3].

At that time, one of the neighbours stated that they informed the local authority which sent experts to examine the house for a cause of this mass illness, and it was found a leakage in gas supply of propane-powered equipment at home and that the indoor level of CO in air was 200 PPM (Part per million).

This history together with the delay in the patient attendance to the Toxicology Unit made a diagnosis of family exposure to CO poisoning with delayed neurologic complications in this patient.

The patient was admitted and full investigations were done. Liver and kidney function tests showed elevated serum ALT, 670 IU/L (Reference range 20- 45 IU/L) [3]; S. bilirubin, 0.8 mg/dl,serum albumin, 3.2 mg/dl; serum creatinine, 4.9 mg/dl; repeated ABG revealed PH7.37, PCO_2 34 mmHg; $PO_2$97.8 mmHg; HCO_3, 24mEq/L; Na 133 mEq/L;K 4.9 mEq/L. At that time, swelling of both lower limbs began to appear and the patient was anuric.

Prompt nephrology consultation was done and decided to begin alkaline diuresis. A workup assessment began and revealed serum CK of 127.000 (Reference value 30 – 308 IU/L). [3] Lower limbs get more swollen, painful, tender, warm and weak.

Doppler US on both lower limbs revealed intact vasculature with no evidence of blood vessel obstruction or thrombosis.

Abdominal ultrasonography revealed that right kidney of the patient is congenitally mal-rotated & small sized with compensatory hypertrophy of the left kidney, and there was increased echogenicity of both kidneys; Grade Ion the left kidney and grade II on the right kidney; then progressed to grade II on both kidneys, with preserved cortico-medullary differentiation (CMD). There was normal appearance of liver, spleen and gall bladder in abdominal US.

From the previous findings, a diagnosis of carbon monoxide poisoning complicated by rhabdomyolysis and subsequent acute renal failure was reached.

As regards to his admitted parents in ICU in another hospital, it was said that one of them has died and the other is still critically-ill and on mechanical ventilation.

The nephrologist recommended doing alkaline diuresis to our patient to enhance elimination of the muscle damage products to avoid their injurious effects on the kidneys. 100 cc of sodium bicarbonate were given with 200 cc normal saline over 2 hours with monitoring of the urine output and the ABG. He recommended also giving 50 cc glucose 25% and 7 units of insulin S.C. over one hour with monitoring for serum K and Na. Repeated ABG showed serum K 7 and urine output was few cc over 2 hours, serum creatinine continued to rise and became 8.5 mg/dl. Hence, there was a condition of pre-renal cause of acute kidney injury (AKI), rising serum creatinine with resistant hyperkalaemia that needed urgent dialysis. A short dialysis session was done, after which there was found a decline of both serum creatinine and potassium levels to 7.8 mg/dl and 4.9mEq/l, respectively.

The patient underwent another 2-hours heparin- free dialysis session after one day.

Renal biopsy was done and revealed acute tubular necrosis (ATN) and myoglobin casts in both kidneys.

Other laboratory studies during that time revealed that complete blood counting, bloodglucose and serum aspartate transaminase (AST) levels were normal.

Follow up of serum creatinine showed level of 9 mg/dl, serum K 4.05 mEq/L and decrease of serum ALT to 513 IU/L and also decrease of serum albumin to 2.8 mg/dl, prolonged prothrombin time, INR 1.2. The patient was still anuric. After 40 mg furosemide infusion, 100 cc of dark brown urine output was reported, analysis of which revealed myoglobin and proteinuria +++. Nephrologists cared of the patient and continued giving 500 ml. normal saline and 80 mg furosemide every 12 hours with ABG monitoring every 6 hours and follow up of serum creatinine / 24 h, to repeat abdominal US and to do non-contrast CT abdomen, to maintain fluid balance and chart provided that intake = output + 200 cc/ 6 h. Nephrotoxic medications were avoided.

However, serum creatinine continued to rise, 9.6 mg/dl; and ALT decreased to 433 IU/L; ABG showed PH, 7.42; K, 3.82 mEq/L; Na 133 mEq/L; HCO_3 21 mEq/L. The patient underwent a dialysis session through a fixed right femoral venous catheter. Ultrasound was repeated and showed Grade II & III increased echogenicity of right and left kidneys, respectively.Haemo-filtration was done and the patient was transferred to the Nephrology care at the Mansoura Nephrology Centre.

Haemodialysis sessions were done day after day, with follow up of serum creatinine and arterial blood gases. The care was continued and the patient began to show improvement after one month; his serum creatinine became 3 mg/dl then continued to decrease until became 1.3 mg/dl (*i.e.* within the normal range). Also ABG and vital signs were stable. The patient was discharged from the Nephrology Centre for out-patient follow-up visits every two weeks and for rehabilitation therapy to regain strength and power of the affected muscles of the lower limbs.

3. Discussion

Carbon monoxide is a leading cause of poisoning morbidity and mortality [1]. It is the third leading cause of accidental poisoning death in the United States [2]. Based on the U.S. national death certificate data, the groups with the highest risk of CO poisoning were male gender and elderly age. The patients' inability to discern CO symptoms remains a cause of increased exposure despite the increased CO detector use [4].

The more significant problem with CO poisoning may be the morbidity rather than the mortality [2]. The most serious complication is persistent or delayed neurologic or neuro-cognitive sequelae, which occurs in up to 50% of patients with symptomatic acute poisonings [5]. Tomaszewski (2006) states that, there is still no completely reliable method of predicting who will have a poor outcome, suggesting that the threshold of hyperbaric oxygen (HBO) therapy for CO poisoning should be appropriately low[2].

Sefer et al. (1999) reported the incidence of rhabdomyolysis and acute renal failure as consequences of acute carbon monoxide poisoning [6]. Also, Janković et al. (2013) listed carbon monoxide among the poisons that can cause muscle injury and fatal rhabdomyolysis, and subsequent renal failure. The authors stated that rhabdomyolysis (RM) is potentially lethal syndrome and that there are no enough published data on its frequency and characteristics in acute poisonings [7].

Carbon monoxide exerts its harmful effects through many mechanisms. Firstly, CO binds to haemoglobin with an affinity 200 to 240 times that of oxygen. Although CO is found in the body as a by-product of haeme degradation, it does not reach the toxic concentration unless inhaled from exogenous sources [2].

This produces maximal shift of oxyhaemoglobin dissociation curve to the left; impairing the ability of haemoglobin to deliver oxygen to the tissues. This enhanced affinity and impaired unloading of oxygen is referred to as the *Haldane effect* [8].

COHb plays only a partial role in the pathogenesis of CO poisoning. Tissue redistribution of CO participates in the severity and mortality rates after CO exposure. This may explain the clinical observation that COHb levels do not correlate with the severity of clinical effects and can be low in the cases of coma from CO poisoning [9].

Moreover, CO has avid affinity to bind to other haeme proteins (cytochromes), such as myoglobin, the cytochrome a-a3 complex of the mitochondrial respiratory chain (cytochrome oxidase), and guanylatecyclase. Myoglobin's affinity for CO is about 30 to 60 times greater than that of oxygen [10]. Binding of CO to myoglobin impairs myocardial oxygen uptake from blood into the mitochondria of tissues. Binding of CO to cytochrome oxidase disrupts cellular respiration and oxygen utilization in all tissues, including the brain. Although cytochrome oxidase binds O_2 with greater affinity than CO, CO competes with oxygen for binding sites under conditions of cellular hypoxia and dissociates slowly from cytochrome oxidase once binding has occurred [9].

Carbon monoxide promotes the production of reactive nitrogen species that further inhibit cellular cytochrome oxidase and electron transport [11]. Cellular hypoxia causes free radical release from vascular endothelial cells and platelets. Concurrently, CO displaces nitric oxide (NO) from heme-containing proteins in endothelial cells and platelets [9]. Once released from cells, NO reacts with free radicals to produce peroxynitrate (ONOO-), which further inhibits cytochrome oxidase, injures DNA and cell membranes, and triggers apoptosis in neuronal tissue [11].

In addition to cellular hypoxia, CO produces smooth muscle relaxation and vasodilatation. CO binds to and stimulates the activity of the haeme protein; guanylatecyclase [9].

This results in increased production of the smooth muscle relaxant, cyclic guanosine monophosphate (cGMP). The displacement of NO from platelets and endothelial cells by CO also results in vasodilatation [9]. NO, also called endothelial derived relaxation factor; is a potent smooth muscle relaxant. Headache from CO poisoning can be explained by extra-cerebral and intra-cerebral vasodilatation. Peripheral vasodilatation partly explains hypotension and syncope from CO poisoning. Also, COHb-induced myocardial ischaemia, direct myocardial depressant effects of CO, and loss of central control of vasomotor tone are effects that can explain hypotension and syncope with CO poisoning.

Clinically, hypotension and syncope (even if transient) signify serious CO exposure and can predict serious neurologic sequelae [12]. It is to be noted that brain areas that have high oxygen requirements and the watershed regions of perfusion (e.g. basal ganglia, hippocampus and subcortical white matter) are particularly susceptible to CO-mediated injury.

Hypoxia and ischaemia are primary CO-induced pathophysiologic processes that induce a cascade of secondary events (ischemia reperfusion effects) that are integral to short- and long-term CO-associated CNS (central nervous system) toxicity [13].

Also, the histopathology of the brain after CO poisoning is similar to that of post-anoxic encephalopathy; so-called 'reperfusion injury' that is largely mediated by oxidative damage [13].

4. Diagnosis [14]

Carbon monoxide (CO) can cause fatal poisoning, however the burden of occult CO poisoning is still unclear.Carbon monoxide (CO) poisoning is responsible for many emergency department (ED) visits during winter months, but it often escapes diagnosis or is misdiagnosed because there are no specific symptoms for CO poisoning.Some patients with CO poisoning may be treated for a myriad of vague acute illness when in reality they have unrecognized CO poisoning and then may suffer more serious and delayed complications.

In this group of patients, in addition to a work-up directed by history, physical examination, laboratory chemistry and blood counts, screening for COHb level will be considered to rule out poisoning by the silent killer gas.

Also, high index of suspicion is needed to exclude mainly cases during the summer months, where the source of CO often remains unknown. A clear consensus on which patients have to be regarded as 'poisoned' is urgently needed in order to allow early treatment and to avoid delayed and serious complications.

Zorbalar et al. (2013) evaluated the ability of (SpCO) as a non-invasive carboxyhaemoglobin measurement method to screen for CO poisoning in these patients. They stated that this method has a screening sensitivity of 82% for CO poisoning, which can aid in diagnosis of suspicious cases of CO poisoning [15].

Moreover, the clinical findings are protean, making diagnosis difficult, and even objective data, such as elevated carboxyhaemoglobin (COHB) concentrations, are not highly prognostic unless at one of the extremes.

Kamisawa et al. (2014) have found a case of CO poisoning with normal COHb level and recommended Magnetic Resonance Spectroscopy (MRS) to be done in these cases. The authors found that MRS demonstrated characteristic findings of leuko-encephalopathy. The white matter of the brain showed suggesting demyelination as an increased choline peak, enhanced anaerobic metabolism as increased lactate and lipids peaks, and reduced neurons as a decreased N-acetyl-aspartate peak, which corresponded to delayed leuko-encephalopathy due to the interval form of carbon monoxide (CO) poisoning [16].

5. Treatment

The mainstay of treatment is initial attention to the airway. Rapid administration of 100% oxygen should be done as soon as possible by either non-rebreather face mask or endo-tracheal tube. It is important to remember that a non-rebreather mask delivers only 70- 90% oxygen; a positive pressure mask or an endotracheal tube is necessary to achieve higher oxygen concentrations. The immediate effect of oxygen is enhancement of the dissociation of COHb. This reduces the half-life of COHb from a mean of 6 hours to about one hour when breathing 100% oxygen at normal atmospheric pressure. The longer elimination half-lives appear to be most often associated with long, low-level exposures [17].

With oxygenation and intensive care treatment, hospital mortality rates for serious exposures range from 1-30%. The duration of treatment is unclear, with a valid endpoint being resolution of symptoms, usually accompanied by COHb< 5% [18].

Suggested indications for HBO after acute CO poisoning are syncope, coma, seizure, altered mental status or confusion, Carboxyhemoglobin> 25%, abnormal cerebellar examination and fetal distress in pregnancy [19].

6. Prevention [20]

Early diagnosis prevents much of the morbidity and mortality associated with CO poisoning, especially in unintentional exposures. Use and increasing quality of home CO-detecting devices will allow personal intervention to prevent CO exposure. If a patient complains that his or her CO alarm sounded, realize that the threshold limit of the alarm is set to approximate a COHb level of 10% at worst. Government ordinances for obligatory CO alarms potentially could prevent many poisonings, particularly during winter storms.

Routine laboratory screening of ED patients during the winter is not efficacious in diagnosing unsuspected CO poisoning. History is the most imortnat clue for diagnosis. Instead, selecting patients with CO-related complaints, such as headache, dizziness, or nausea, increases the yield to 5- 11%. During winter, risk factors such as gas heating or symptomatic cohabitants in patients with influenza-like symptoms (e.g., headache, dizziness, nausea) will be the most useful method for deciding when to obtain COHb levels in potential cases.

Checking for equipments is important to prevent CO leak. One source of exposure to this insidious poison is use of propane-powered equipments, like what occurred in this case.

7. Conclusion

Carbon Monoxide poisoning remains one of the most common causes of mortality and morbidity in Egypt. Education of the public and increasing orientation of the sources of exposure, manifestations of poisoning and methods of prevention are of paramount importance to decrease burden of exposure to the silent killer gas. Early suspicion and timely intervention of the affected victims are mandatory to save lives and prevent/manage complications.

Abbreviations

ABG, Arterial Blood Gases; CO, Carbon Monoxide; ED, Emergency Department; HBO, Hyperbaric Oxygen Therapy.

Competing Interests

The authors declare that they have no competing interests regarding the focus, interest or any of the contents of this manuscript.

Source of Funding

No source of funding was present writing, submission or any stage of this article preparation.

References

[1] Lavonas E. J.: Carbon Monoxide Poisoning. In: Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose, 4th ed., 2007, Shannon, M. W., Borron, S. W. and Burns, M. J., Eds., Elsevier, publisher. Ch. (87). P. p. 1297-1307.

[2] Tomaszewski C. "Carbon Monoxide". In: Goldfrank's Toxicologic Emergencies, 8th ed., Flomenbaum, Neal E.; Goldfrank, Lewis R.; Hoffman, Robert S.; Howland, Mary Ann; Lewin, Neal A.; Nelson, Lewis S. Eds., 2006, McGraw-Hill publisher. Ch. (120). P.p. 1689-1703.

[3] White DB, Curtis JR, Wolf LE, Prendergast TJ, Taichman DB, Kuniyoshi G, Acerra F, Lo B, Luce JM. Life support for patients without a surrogate decision maker: who decides?. *Ann Intern Med*. 2007; 147(1): 34-40.

[4] Centres for Disease Control and Prevention. Non-fatal, unintentional, non-fire related carbon monoxide exposures-United States, 2004-2006. *MMWR Morbid. Mortal. Wkly Rep*. 2008; 57: 896-899.

[5] Weaver LK, Hopkins RO, Chan KJ,Churchill S, Elliott CG, Clemmer TP, Orme JF Jr, Thomas FO, Morris AH.Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med*. 2002; 117: 801-808.

[6] Sefer S, Degoricija V, Bilić B, Trotić R, Milanović-Stipković B, Ratkovi-Gusić I, Kes P. Acute carbon monoxide poisoning as the cause of rhabdomyolysis and acute renal failure. *Acta Med Croatica*. 1999; 53(4-5): 199-202.

[7] Janković SR, Stosić JJ, Vucinić S, Vukcević NP, Ercegović GV. Causes of rhabdomyolysis in acute poisonings. *Vojnosanit Pregl*. 2013. 70 (11): 1039-45.

[8] Huang, L. E.; Willmore, W. G.; Gu, J.; Goldberg, M. A. andBunn, H. F., Inhibition of hypoxia-inducible factor 1 activation by carbon monoxide and nitric oxide. Implications for oxygen sensing and signalling". *J. Biol. Chem.* 1999; 274 (13): 9038-9044.

[9] Huzar, T. F.; George, T. andCross, J. M., Carbon monoxide and cyanide toxicity: etiology, pathophysiology and treatment in inhalation injury. *Expert Rev Respir Med.*, 2013; 7 (2): 159-170.

[10] Szponar, J.; Kołodziej, M.; Majewska, M.; Zaleski, K. andLewandowska-Stanek, H., Myocardial injury in the course of carbon monoxide poisoning. *PrzeglLek.*, 2012; 69 (8): 528-534.

[11] Bild, W.; Ciobica, A.; Padurariu, M. andBild, V., The interdependence of the reactive species of oxygen, nitrogen, and carbon. *J PhysiolBiochem.* 2013; 69 (1): 147-154.

[12] Aksu, N. M.; Akkaş, M.; Çoşkun, F.; Karakiliç, E.; Günalp, M.; Akküçük, H.; Ataman, D. K.; Özcan, H.; Özmen, M. M., Could vital signs predict carbon monoxide intoxication?. *J Int Med Res.* 2012; 40 (1): 366-370.

[13] Ruth-Sahd, L. A.; Zulkosky, K.and Fetter, M. E., Carbon monoxide poisoning: case studies and review. *DimensCrit Care Nurs.* 2011; 30 (6): 303-314.

[14] Kao, L. W. and Nañagas, K. A., Carbon monoxide poisoning. *Med Clin North Am.* 2005, 89 (6): 1161-1194.

[15] Zorbalar, N.; Yesilaras, M. and Aksay, E., Carbon monoxide poisoning in patients presenting to the emergency department with a headache in winter months. *Emerg Med J.* 2013, Epub ahead of print.

[16] Kamisawa, T.; Ikawa, M.; Hamano, T.; Nagata, M.; Kimura, H. andYoneda, M., A case of interval form of carbon monoxide poisoning without increased carboxyhemoglobin level diagnosed by characteristic MR spectroscopy findings. *RinshoShinkeigaku.* 2014, 54 (3): 234-237.

[17] Kudo K, Otsuka K, Yagi J, Sanjo K, Koizumi N, Koeda A, Umetsu MY, Yoshioka Y, Mizugai A, Mita T, Shiga Y, Koizumi F, Nakamura H, Sakai A. Predictors for delayed encephalopathy following acute carbon monoxide poisoning. *BMC Emerg Med.*, 2014, 14: 3.

[18] Ilano AL, Raffin TA. Management of carbon monoxide poisoning. *Chest*. 1990, 97 (1): 165-169. Cited from: Tomaszewski C. "Carbon Monoxide". In: Goldfrank's Toxicologic Emergencies, 8th ed., Flomenbaum, Neal E.; Goldfrank, Lewis R.; Hoffman, Robert S.; Howland, Mary Ann; Lewin, Neal A.; Nelson, Lewis S. Eds., 2006, McGraw-Hill publisher. Ch. (120). P. 1694.

[19] Buckley NA, Isbister GK, Stokes B, Juurlink DN. Hyperbaric oxygen for carbon monoxide poisoning: a systematic review and critical analysis of the evidence. *Toxicol. Rev.*, 2005; 24 (2): 75-92.

[20] Boehmer TK, Foster SL, Henry JR, Woghiren-Akinnifesi EL, Yip FY; Centers for Disease Control and Prevention (CDC). Residential proximity to major highways - United States, 2010. *MMWR SurveillSumm.* 2013, 62 Suppl. 3: 46-50.