

Chronic respiratory carbon dioxide toxicity: a serious unapprehended health risk of climate change.

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Abstract

As atmospheric levels of carbon dioxide continue to escalate as a driver of climate change, the issue of CO₂ toxicity is not recognised as a global risk by the science community. The toxicity of CO₂ for breathing has been well defined for high concentrations but it remains effectively unknown what level will compromise human health when individuals are exposed for their whole life. There is evidence from the few studies of long-term low-level exposure that permanent exposure, to CO₂ levels predicted by the end of the century, will have significant effects on humans. Other studies of slightly higher CO₂ levels may offer clues to effects, not yet observed, that may occur when humans experience lifelong exposure. Although humans and animals are able to deal with elevated levels of CO₂ in the short-term due to various compensation mechanisms in the body, the persistent effects of these mechanisms may have severe consequences in a perpetual environment of elevated CO₂. These include threats to life such as kidney failure, bone atrophy and loss of brain function. Existing research also indicates that as ambient CO₂ increases in the near-future, there will be an associated increase in cancers, neurological disorders and many other conditions. Research is urgently required to clearly identify the severity and proximity of this risk, associated with the primary human function of breathing, being a potential major aspect of climate change.

Introduction

Carbon dioxide is one of the most frequently overlooked of all toxic gases. Even to refer to CO₂ as a toxic gas is a surprise to many safety professionals (Henderson 2006). In indoor environments CO₂ concentration is often elevated relative to ambient outdoor levels due to the fact that the exhaled breath from humans contains high levels (about 4 %) and ventilation may not be adequate to prevent the resulting increase in CO₂ levels. Despite the possible adverse effects on the health where many people occupy buildings or vehicles, there is very low awareness of this issue in the general community.

At present the average ambient concentration of CO₂ (in fresh air) is about 400 ppm (Carbon Dioxide Information Analysis Center 2015). There is now very strong scientific evidence that carbon dioxide (CO₂) levels in our atmosphere are rapidly and consistently increasing in an uncontrolled manner due to humanity's activities, largely resulting from the burning of fossil fuels (Figure 1).

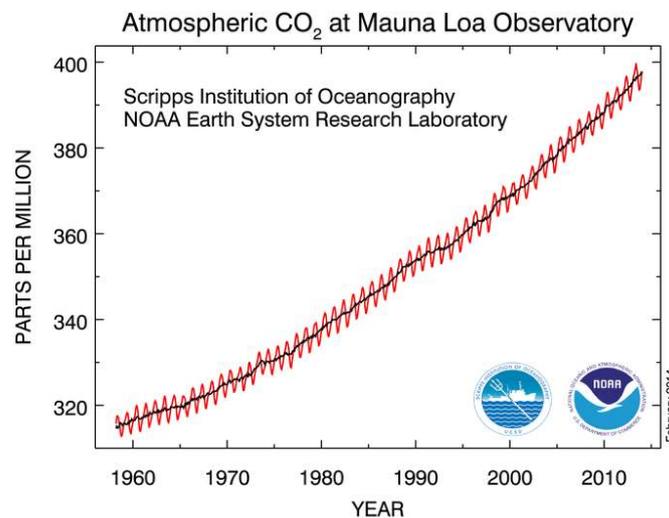


Figure 1. The rapid increase of CO₂ in the atmosphere since the start of direct measurements at Mauna Loa Observatory, Hawaii.

Early primate ancestors of humans evolved about 28 million years ago. Throughout this period of human evolution CO₂ levels in the ambient atmosphere remained relatively stable at levels below 300 parts per million (ppm) (Eggleton 2013; Beerling and Royer 2011). This is derived from a combination of studies of relict features including air trapped in ice cores, the stomata density of fossil leaves as well as the composition of fossil plankton and soils. Since about 1820, CO₂ levels have rapidly increased and are now above 400 ppm (Figure 1). This is a potentially catastrophic problem for many species of animals, including humans, for a number of reasons. The most well publicised issue is that of climate change. The mechanisms and history of global warming associated with CO₂ increase are well understood and the increase in atmospheric energy gradients will produce more extreme temperatures and weather events. Climate change itself may not appear to be catastrophic to many people – for example, it might be possible to escape the effects of even a 5 degree C increase this century by moving to a cooler and safer geographic location. However, it is possible that humans have overlooked the more direct and immediate toxicity aspect of increasing atmospheric CO₂. The earth's atmosphere has already reached CO₂ levels that are outside the range

breathed by humans throughout their evolution. As well, some studies have defined the role of elevated atmospheric CO₂ in historical mass extinction events (Knoll et al. 1996)

We know that breathing CO₂ is toxic to humans when levels are high with numerous deaths reported based on occupational exposure (Scott et al. 2009). Although the CO₂ exposure limit for an 8 hour working day has been set at 5,000 ppm (OSHA 2012), this limit was decided in 1946 and based on relatively short-term observations of fit and healthy submariners (Scott et al, 2009). The safe level for lifetime exposure may be significantly lower than this and a number of researchers suggest there could be toxicity effects at CO₂ levels predicted in the near future with ongoing anthropogenic emissions (Portner et al. 2004; Robertson 2006; Ezraty et al. 2011; Antic 2012; McNeil and Sasse 2016). So the question is: how long will it take, at present and future rates of increase, to reach levels that will impact on human health, no matter where you live, over a lifetime? To answer this question, the safe level of CO₂, for continuous breathing in humans, needs to be determined. This paper is an attempt to evaluate available knowledge and to examine the likely and possible risks for the near to medium-term future.

The role of carbon dioxide in breathing

Breathing is one part of physiological respiration and is required to sustain life (Raven et al. 2007). Aerobic organisms such as birds, mammals, and reptiles, require oxygen to release energy by cellular respiration, through the metabolism of molecules such as glucose. During aerobic respiration, glucose is broken down by oxygen to release energy, while carbon dioxide and water are the by-products of the reaction. Breathing delivers oxygen to where it is needed in the body and removes carbon dioxide thereby exchanging oxygen and carbon dioxide between the body and the environment. Carbon dioxide (CO₂) is essentially a waste product of the body but is important as a feedback mechanism by helping to regulate the rate of breathing (Patton and Thibodeau 2009) since the blood level of CO₂ acts directly on the respiratory centres in the brain stimulating the nerves that activate the respiratory muscles. High levels of carbon dioxide correspond with high levels of acid (low pH) in the blood and signal the need for more exchange with oxygen. The exchange of oxygen and CO₂ between the lung alveoli and the blood occurs by simple diffusion - oxygen diffusing from the lung alveoli into the blood and CO₂ from the blood into the lung alveoli depending on the concentration (or pressure) of both oxygen and CO₂ in the alveoli. We do this, of course, by breathing - continuously bringing fresh air (with a lot of oxygen and little CO₂) into the lungs and alveoli.

So there is an optimal range for the concentrations of CO₂ in the air we breathe. Too little can mean that breathing is too slow and not enough oxygen is brought into the body. But too much can compromise our ability to remove CO₂ from our bodies as a waste product. So what are the effects of too much CO₂ and what is the level that can cause health problems in humans?

Health effects from short term exposure to high levels of CO₂

Breathing too much CO₂ results in high levels of CO₂ in the blood (hypercapnia) associated with a decrease in blood pH. This results in a condition known as acidosis. The decreases in blood and tissue pH produce effects on the respiratory, cardiovascular, and central nervous systems (CNS)

(Eckenhoff and Longnecker 1995). Changes in pH act directly and indirectly on those systems producing effects such as tremor, headache, hyperventilation, visual impairment, and CNS impairment. In terms of worker safety, the US Occupational Safety and Health Administration has set a permissible exposure limit (PEL) for CO₂ of 5,000 parts per million (ppm) (or 0.5 %) over an 8-hour work day (OSHA 2012). They report that exposure to levels of CO₂ above this can cause problems with concentration, an increased heart rate, breathing issues, headaches and dizziness.

Exposures to 1-5 % CO₂ for short-term periods have been documented to produce symptoms on humans and animals such as dyspnea (shortness of breath), modified breathing, acidosis, tremor, intercostal pain, headaches, visual impairment, lung damage, increased blood pressure, bone degradation, reduced fertility, alterations to urine and blood chemistry as well as erratic behaviour (Halperin 2007; Rice 2004; Guais et al. 2011; Schaefer et al. 1963; Yang et al. 1997). In humans, these levels of CO₂ also induce panic attacks, interrupt the processes of metabolic enzymes and disrupt normal cell division processes (Colasanti et al. 2008; Guais et al. 2011; Abolhassani et al. 2009).

Health risks to humans continue to escalate, with progressively higher CO₂ concentrations causing more severe reactions and faster responses. A value of 40,000 ppm is considered immediately dangerous to life and health given that a 30-minute exposure to 50,000 ppm produces intoxication, and concentrations around 70,000 ppm produce unconsciousness (NIOSH 1996). Additionally, acute toxicity data show the lethal concentration for CO₂ is 90,000 ppm (9%) for a 5 minute exposure.

Physiological compensation for elevated CO₂

When considering long-term effects of breathing sustained elevated CO₂, it is important to consider compensation mechanisms in the body, that regulate for increased CO₂ and acidity in the blood, and how these change over time with persistent exposure. The blood pH changes trigger various compensatory mechanisms, including pH buffering systems in the blood, increased breathing to reduce excess CO₂ in the bloodstream, increased excretion of acid by the kidneys to restore acid-base balance, and nervous system stimulation to counteract the direct effects of pH changes on heart contractility and vasodilation (widening of the blood vessels) (Burton 1978; Eckenhoff and Longnecker 1995). In respiratory acidosis, for a period the kidneys retain bicarbonate helping to normalise the pH of the blood as it passes through them. This occurs within 6 to 8 hours of exposure but achieves full effect only after a few days. With continued high levels of CO₂ in the blood, metabolic acidosis occurs and the kidneys don't respond in producing bicarbonate (Schaefer et al 1979a). After this the body uses the bones to help regulate the acid levels in the blood. Bicarbonate and a positive ion (Ca²⁺, K⁺, Na⁺) are exchanged for H⁺. Over chronic periods of acidosis, bicarbonate and elements are released from the bones resulting in bone breakdown with calcium mobilised to the kidneys. This aspect is discussed further later.

Health effects at common indoor CO₂ concentrations

There is a large recent volume of literature that has documented the occurrence and levels of CO₂ in classrooms across the world including kindergartens, day-care centres, primary schools, high schools and universities (Bako-Biro et al 2011; Widory and Javoy 2003; Kukadia et al. 2005; Dijken et al. 2005; Branco et al. 2015; Heudorf et al. 2009; Santamouris et al. 2008; Ferreira and Cardoso 2014;

Gaihre et al. 2014; Jurado, et al. 2014; Lee and Chang 2000; Muscatiello et al 2015; Carreiro-Martins et al. 2014). There is general agreement that the levels of CO₂ in classrooms commonly (20-50% of all classrooms) exceed 1,000 ppm and are often much higher, sometimes reaching levels as high as 6000 ppm for extended periods. A number of studies have identified CO₂ associated symptoms and respiratory diseases such as sneezing, rales, wheezing, rhinitis, and asthma (Carreiro-Martins et al. 2014; Ferreira and Cardoso 2014). Other symptoms, cough, headache, and irritation of mucous membranes, were also identified (Ferreira and Cardoso 2014). Lack of concentration was associated with CO₂ concentrations above 1000 ppm. Gaihre et al. (2014) found that CO₂ concentrations exceeding 1000 ppm is associated with reduced school attendance. Teachers also report neuro-physiologic (i.e., headache, fatigue, difficulty concentrating) symptoms at CO₂ levels greater than 1000 ppm (Muscatiello et al. 2015).

Offices have similar levels of CO₂ to classrooms depending on the number or density of workers and the types of ventilation systems (Lu et al. 2015; Tsai et al. 2012, Seppanen et al. 1999). These studies have found strong evidence of the relationship between CO₂ levels in offices and Sick Building Syndrome (SBS) health effects such as headaches, dizziness, fatigue, respiratory tract symptoms, eye symptoms, nasal and mucous membrane symptoms (Seppanen et al. 1999; Lu et al. 2015; Tsai et al. 2012). Seppanen et al. 1999 conducted a review of available literature and were careful to eliminate other confounding airborne building contaminants. The reviewed studies included over 30,000 human subjects, and they concluded that the risk of SBS symptoms decreased significantly with carbon dioxide concentrations below 800 ppm. Whether CO₂ itself is responsible for the health symptoms is still a subject of debate since historically it has been assumed, despite lack of direct evidence, that other airborne contaminants are the cause (Zhang et al. 2016).

Although not studied for health effects, vehicles can often contain even higher levels of CO₂ particularly where there are multiple passengers for relatively long journey times. CO₂ levels can build up to 5,000 ppm after less than an hour of driving with two people in a car with only internal air (Gładyszewska-Fiedoruk 2011). Buses with high numbers of passengers consistently reach average CO₂ concentrations of > 2500 ppm (Chiu et al 2015). Airliners can contain levels of around 2000 ppm for the duration of the flight (Gładyszewska-Fiedoruk 2012). Measurements on an Italian submarine showed a steady increase to 5000 ppm CO₂ after 2 hours of being submerged (Ferrari et al. 2005). Extremely high CO₂ concentrations (10,000-20,000 ppm) are commonly found inside motorcycle helmets in both stationary and moving situations (Bruhwiler et al. 2005).

There is increasing concern about the effect of CO₂ on learning and cognitive abilities relating to schools and offices. Testing of students has found that CO₂ can negatively affect attention, memory, concentration and learning ability affecting academic performance (Bako-Biro et al. 2011; Coley et al. 2007). Two recent university studies of cognitive effects of CO₂ were notable in their strong research design (Satish et al 2012; Allen et al 2015). They showed that low level CO₂ (between 950 ppm and 2500 ppm CO₂) affected the cognitive abilities of students and information professionals in the indoor environment. Satish et al. (2012) tested only variations in CO₂ over periods of 2.5 hours of exposure. For seven of nine scales of decision-making performance (basic activity, applied activity, task orientation, initiative, information usage, breadth of approach, and basic strategy), performance was significantly impaired in a dose-response manner with higher CO₂ levels. For example, compared with mean raw scores at 600 ppm CO₂, mean raw scores at 1,000 ppm CO₂ were 11–23% lower, and

at 2,500 ppm CO₂ were 44–94% lower. As part of a larger study that included volatile organic compounds (VOCs), Allen et al. (2015) found that, after CO₂ was independently modified (from a baseline of 480-600 ppm) for individual 8 hour exposures, cognitive function scores were 15% lower at 950 ppm and 50% lower at 1400 ppm. This study used similar methodology to score cognitive function and the results largely repeated the findings of the earlier work (Satish et al 2012). However one difference was that, at 1500 ppm CO₂, even focussed activity was found to have declined (Allen et al 2015). A third study found similar negative effects on human cognitive abilities, in experiments involving 140 minute sessions, as well as increased fatigue at levels of 3000 ppm CO₂ compared with 600 ppm (Kajtar and Herczeg 2012). This study also measured some physiological parameters with heart rate analysis suggesting significantly increased mental effort at 3000-4000 ppm. A more recent study (Zhang et al. 2016) has suggested that none of these effects are due to CO₂ and that human bioeffluents are the likely cause. This was based on experiments that showed no cognitive impairment in humans when high CO₂ levels were artificially supplied but significant effects when the CO₂ was due to human respiration with the latter case assumed to allow the associated build-up of human bioeffluents. Zhang et al (2016) appear to recognise that their results contradict those of the previous three studies which found cognitive impairment using artificially supplied CO₂. They argue that the studies of Satich et al (2012) and Allen et al (2015) involved cognitive testing was too complex for the type of thinking that would be required in a normal indoor environment. However, this criticism of previous work appears to be irrelevant to the issue. Given that Zhang et al. (2016) used fairly simple cognitive tests, and that their conclusions disagree with previous relevant studies and generally support earlier untested theories about the causes of sick building syndrome, the paper might be flawed. Nevertheless, further studies of the effect of CO₂ on cognitive impairment and human well-being are needed.

There are also indoor situations where exhaled human breath and restricted air flow can produce extreme and dangerous levels of CO₂. For example infant deaths have been associated with level of up to 8% (80,000 ppm) CO₂ based on modelling for an infant covered by blankets (Campbell et al. 1996).

Health effects from continuous long term exposure to lower elevated levels of CO₂

Where indoor levels of CO₂ are relatively high and affecting health, it is generally possible to obtain relief by going outdoors. However this may not be the case in a climate change future where ambient CO₂ is persistently high and effects of continuous long-term exposure must be considered. There have been very few studies related to long-term exposure at lower CO₂ levels, elevated above ambient, perhaps for logistical reasons since it is difficult to arrange an experiment for the duration of a human life-span. We are looking for information on the effect on humans of CO₂ levels at 1,000 ppm or less – noting that this is the level that some feasible models predict could be reached in the ambient atmosphere in less than 100 years (Smith and Woodward 2014). Given the lack of research at these CO₂ levels, it seems reasonable to examine the research available for medium-term studies on levels of CO₂ less than 10,000 ppm (1%). A good place to look is the safety guideline documents for activities where humans are required to remain in enclosed spaces for long periods such as spacecraft and submarines.

NASA sought to determine the safe levels for long-term exposure to CO₂, in spacecraft and submarines, but found little research focused on levels below 10,000 ppm CO₂; as such, there was no definitive study available to guide standards (Cronyn et al. 2012). They set the maximum allowable CO₂ concentration limits, for long term (1,000 day) habitation of submarines and spacecraft, at 5000 ppm (James and Macatangay 2009). International Space Station (ISS) crew members have repeatedly reported symptoms associated with acute CO₂ exposure at levels of 5,000 to 6,600 ppm CO₂. Headache was the most commonly reported symptom; other symptoms reported included lethargy, mental slowness, emotional irritation, and sleep disruption (Law et al. 2010). For space flight, Cronyn et al. (2012) identified three potential areas of operational impact of low level CO₂: renal calculi (kidney calcification) and bone reabsorption; cerebral blood flow; and mission performance. With no definitive research to provide insight into these areas, further evaluation was recommended to examine the effects of various low-to-moderate CO₂ concentrations (from ambient levels up to 1%) on human subjects.

Studies of CO₂ effects on humans in enclosed submarines have been reviewed by the US government (Halperin 2007) although again most of these studies are for high (> 1%) CO₂ levels at relatively short exposure durations. At these levels (>1%), many of the debilitating and acute symptoms described above were noted. Current safe levels for continuous exposure in submarines were deemed to be around 5,000 ppm CO₂ – this level is set arbitrarily at one third of the level where there were obvious signs of health problems (James and Macatangay 2009). It was also noted that if problems are observed, a submarine can surface so that its occupants can be exposed to the ambient atmosphere. Halperin (2007) reports that exposures to CO₂ levels as low as 7,000 ppm can lower blood pH by up to 0.05 units and induce renal (kidney) compensation in healthy subjects. This compensation occurs over a variable period of time, but effects of lowered pH on clinical status or performance have not been reported either experimentally or operationally. Given that kidney compensation cannot occur indefinitely, there is some doubt about whether submariners could sustain the “safe” level of 5,000 ppm CO₂ if they spent years exposed to it.

Other serious effects related to the body’s compensation activities under persistent exposure have been observed at or less than 10,000 ppm CO₂ including lung dead space volume, kidney calcification, decreased bone formation and increased bone resorption (Rice 2004; Schaefer et al., 1979). As part of a US Navy experimental program in the 1960’s and 1970’s investigating impacts of long-term CO₂ exposure, Schaefer (1979) found that, in a study of Guinea pigs in an enclosed environment breathing 5,000 ppm CO₂ for 8 weeks, under these conditions the kidneys started to calcify with the calcium having been released from bone. Schaefer (1982) also indicated that preliminary experiments have found kidney effects in animal studies for CO₂ concentration as low as 2,000 ppm.

Other important physiological CO₂ effects on health

Cerebral blood flow (CBF) effects from breathing CO₂ is a significant issue for humans. As CO₂ in the blood increases, CBF increases to effectively wash out CO₂ from brain tissue and helps regulate central pH (Ainslie and Duffin, 2009). In a 23 day experiment on humans, Sliwka et al. (1998) found that cerebral blood flow is increased in the presence of 7,000 ppm (0.7%) CO₂ by as much as 35%

and that CBF remained elevated until the end of the evaluation period, 2 weeks after the exposure. The impacts of persistent increase in CBF are unclear although there may be a risk of raised intracranial pressure (ICP) which can compress and damage delicate brain tissue. There is also evidence that the CBF response to increased CO₂ is impaired in Alzheimer's patients and that this is linked to the decline in cognitive abilities (Glodzik et al 2013) which will worsen as CO₂ in the atmosphere increases.

In humans, carbon dioxide is also known to play a role in oxidative stress caused by reactive oxygen species (ROS) (Ezraty et al. 2011). ROS are produced by aerobic metabolism of molecular oxygen and play a major role in various clinical conditions such as malignant diseases, diabetes, atherosclerosis, chronic inflammation and neurological disorders such as Parkinson's and Alzheimer's diseases (Waris and Ahsan 2006). In particular, oxidative damage to cellular DNA can lead to mutations resulting in the initiation and progression of cancer. Ezraty et al (2011) demonstrated that current atmospheric CO₂ levels play a role in oxidative stress and that increasing CO₂ levels between 400 and 1,000 ppm increasingly exacerbated oxidative stress and damage to DNA in bacteria. Increased CO₂ increases the production of ROS leading to increased incidence of cancers and other diseases including the promotion of virus activity. Ezraty et al (2012) concluded that with increasing atmospheric CO₂ concentrations, this exacerbation might be of great ecological concern with important implications for life on Earth.

Similar to cancer there are a number of conditions where some individuals are currently impacted by the effects of CO₂ toxicity. One example is people affected by sleep disordered breathing (SDB). Brillante et al (2012) found that the development of nocturnal hypercapnia in normal indoor CO₂ air concentration, quantitated by a large difference in carbon dioxide in the blood between morning and evening, predicted increased mortality in SDB patients. This is a result of the lack of efficacy of an individual's respiratory regulatory system in sleep for maintaining normal blood gas tensions (Brillante et al. 2012). As CO₂ levels in the atmosphere increase into the future, the impacts on and number of affected individuals will logically increase.

Another study (Goromosov 1968) showed harmful physiological effects on humans at only 1,000 ppm CO₂ reporting changes in respiration, circulation, and cerebral electrical activity.

Discussion

The main question here is: what is the direct risk to the human species posed by the breathing of ambient atmospheric CO₂ concentrations that are rapidly increasing? More specifically, what is the effect on physiology and what is the level of ambient atmospheric CO₂ that provides unacceptable risk? If this level is reached in the near future, the global human society should be concerned. Some climate models suggest that atmospheric CO₂ levels could be as high as 1,000 ppm in this century – this is completely unknown for the whole primate evolutionary lineage which has only ever experienced levels below and up to the current level of 400 ppm.

As observed in this paper, there is no documentation of long term physiological studies of exposure to 1,000 -2,000 ppm CO₂ or less. However, there are short-term exposure studies describing disease symptoms at levels around 1000 ppm CO₂ and reduced cognitive ability in humans at around 800

ppm CO₂. The studies of cognitive effects were conducted at CO₂ levels that represent typical conditions currently present in offices, classrooms and apartments. Although the modest reductions in multiple aspects of decision making, seen as low as 950 ppm (Allen et al. 2015), may not be critical to individuals, at a societal level, or for employers, an exposure that reduces performance even slightly could be economically significant. Surprisingly it is possible that such effects occur without recognition in daily life (Satish et al. 2012). It appears that the CO₂ induced decline in cognitive ability is due to increased Cerebral Blood Flow (CBF) and the resulting effects on central nervous system and brain cortical function (Satish et al 2012; Glodzik et al 2013). The effect on cortical function is supported by a study of infants that showed an inverse relationship between blood CO₂ and electrocortical activity (Wikstrom et al. 2011).

The impacts on students including sickness, reduced attendance and reduced learning abilities should be a concern for society. Moreover, the relatively high levels of CO₂ in vehicles associated with declining concentration and fatigue has serious implications for the safety of drivers and their passengers. This is an issue that does not appear to have been raised in research on driver fatigue illustrating the general lack of awareness about CO₂ effects.

Most of the problems associated with elevated indoor CO₂ levels greater than about 800 ppm, can be alleviated by spending time in fresh air. The indoor environments can be restored to acceptable CO₂ levels with effective ventilation although this is often not being achieved. The available resource of fresh air may be the underlying misguided reason why there is a lack of concern for pollution and its effects. Significantly this resource may not be available in the future as rising atmospheric CO₂ associated with climate change may exceed the 800 ppm level in the current century (Smith and Woodward, 2014). At that stage, there will be no outdoor escape from the described symptoms. It seems possible, even likely, that under such a condition of permanent exposure, there may be health impacts at levels below that where obvious effects are observed, i.e. less than 800 ppm.

As mentioned previously the body compensates for high levels of CO₂, through a combination of increased breathing, blood pH buffering, kidney and bone adaptations depending on the length of continuous exposure, until we can resume breathing lower levels of CO₂. There are very few studies that indicate what level of CO₂ in the air will induce the longer-term compensation activities. Kidney involvement has been documented to occur in animals at 2,000 ppm (Schaefer 1979) and 7,000 ppm in humans (Halperin 2007) although no lower limits were defined. One author suggests that blood pH would be reduced to dangerous levels, if there were no physiological compensation, at CO₂ levels as low as about 430 ppm (Robertson 2006) implying that compensation would occur at this level. Ambient conditions may already be dangerously close to CO₂ levels that will induce continuous body compensation. Moreover, there is strong evidence that, with chronic activity, compensation mechanisms can produce serious health issues such as kidney calcification and bone loss. There are known health problems associated with persistent body compensation for blood acidity at CO₂ levels that are about 10 times the current ambient air concentration, but these are for a relatively short duration studies. Although studies are lacking, it is conceivable that these problems might appear at much lower levels of CO₂ if compensation persisted for a much longer periods, for example living a whole lifetime in an elevated CO₂ atmosphere of a climate changed future. In the final paper of the US Navy CO₂ research program, Schaefer (1982) indicated that this issue had “become the concern of the Department of Energy and other US government agencies” although it appears to have been

largely forgotten since. If allowed to persist, problems such as kidney calcification could lead to renal failure. In the extreme case lifespans could become shorter than the time required to reach reproductive age. This would result in extinction of the species without interventions such as the creation of artificial living environments.

While this sounds alarmist, the fact remains that the level of CO₂ in the ambient atmosphere, beyond which the health or survival of the species could be threatened, remains unknown. This is surely an unacceptable risk. The current evidence that the human species is already impaired in indoor environments this is likely to get worse as rising outdoor levels of CO₂ contribute to increased indoor concentrations. Furthermore, the incidence and prevalence of human kidney calcification (i.e. stones) is increasing globally with the rate highest for males (Romero et al. 2010). Although this may not be related, it is possible that rising office levels of CO₂ is a contributing cause. As well there is evidence that CO₂ toxicity contributes to a range of serious health issues including cancer, neurological diseases and sleep disorders, is being experienced by individuals at the current ambient levels which are now 40% higher than pre-industrial levels. It seems likely that CO₂ toxicity related to human-induced climate change is already having an impact on population health but not yet recognised.

Of course it is not only humans that are at risk. It has been demonstrated that animals have varying degrees of susceptibility to carbon dioxide (Schaefer et al. 1971). The impacts of elevated CO₂ are even greater for water breathing animals than air breathing animals. In general, land animals have much higher blood CO₂ than aquatic animals and can compensate for hypercapnia by increasing ventilation. In aquatic animals, compensation by increased ventilation is rare and a small increase in ambient CO₂ causes hypercapnic acidosis (Portner et al. 2004; Knoll et al. 1996; McNeil and Sasse 2016). Studies have shown that hypercapnia in fish produces substantial neurological, behavioural and physiological effects for even short term exposures at a CO₂ concentration predicted to be persistent in the ocean before the year 2100; this level corresponding with an atmospheric concentration of 650 ppm CO₂ (McNeil and Sasse 2016).

So why is the issue of CO₂ respiration toxicity related to near-future ambient atmosphere concentrations not being addressed? Despite significant documentation of health issues due to CO₂ in indoor environments, there is very low awareness in the community. For spacecraft and submarines there are practical considerations that influence the recommended safe levels. Initial safe limits for the International Space Station were partly decided by engineering requirements (Cronyn et al. 2012) and submarine limits were balanced by the ability to surface and renew air quality. It seems that there has been little concern about low-level toxicity of CO₂ because we have always had the back-up of an ambient atmosphere with low levels of CO₂. It is also possible that climate change has become the main focus of rising CO₂ levels and there is a lack of perception amongst scientists about the potential dangers of CO₂ toxicity. The latest IPCC report on climate change states that CO₂ is not considered a health damaging air pollutant at lower levels of concentration (Smith and Woodward 2014) although these levels are not defined. The IPCC report did however describe the findings of Satich et al. (2012) as a reported “reduction in mental performance at 1,000 ppm CO₂ and above, within the range that all of humanity would experience in some extreme climate scenarios by 2100” (Smith and Woodward 2014). Moreover, CO₂ toxicity is very much a discipline of environmental medicine which has not focussed on the potential problem

because chronic toxicity cases have not yet been recognised; this may be a reason why there are very few researchers involved at this stage.

Conclusions

The main aim of this paper was to explore the question of toxicity for human breathing at levels of CO₂ that could be attained with the continued unabated rise in atmospheric CO₂ associated with climate change. For humans, breathing is paramount before finding water, food and shelter. From the evidence presented here, there appears to be current health impacts of rising CO₂ levels and a significant risk of serious health issues arising in the human population at some time in this century.

Current impacts of elevated and increasing ambient CO₂ in indoor environments include respiratory diseases, headaches, fatigue and other symptoms at levels above 800 ppm. This finding together with the impairment of cognitive abilities at CO₂ levels just above ambient (between 600 and 1,000 ppm) is significant in that it has implications at a societal level for human function particularly for jobs with critical responsibility (e.g. surgery, air-traffic controllers, drivers etc.) together with the impact on learning, human development and economies. These impairing CO₂ effects will be increased and more permanent in a future with elevated outdoor ambient CO₂ concentrations. Other ongoing impacts may include the exacerbation by CO₂ of cellular oxidative stress resulting in an increase in cancers, neurological diseases, viruses and many other conditions. Studies of health effects at higher levels of CO₂ at around 2,000-5,000 ppm demonstrate the impact of persistent attempts by the body to compensate for increased acidity in the blood. These effects include kidney calcification, bone degradation and cerebral blood flow disorders. The latter can be related to a decrease in cognitive abilities and potential brain damage. While there is a lack of studies in humans at lower CO₂ levels, demonstrated effects in animals and symptoms experienced by humans indicate that longer-term mechanisms compensating for increased blood CO₂ might be active when breathing at around 800-1000 ppm CO₂. This is a level predicted for the ambient atmosphere by the end of the century in a “business as usual” world. This means that most humans could at this time be experiencing persistent body compensation for acidosis effects resulting in serious health problems that may threaten species viability. The risk for near-future human and animal population health is extremely high and should be communicated since global awareness of this issue may enable a change practice on CO₂ emission activities. Also, new research on the health effects of long term exposure to realistic future atmospheric CO₂ levels is urgently needed.

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