Micro Air Embolism Contribution to Blast-Induced Mild Traumatic Brain Injury

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INTRODUCTION

Massive air embolism (AE) from lung disruption is the accepted principal etiology of mortality in blast injury (White et al., 1971; Sharpnack, Johnson & Phillips, 1990). For sub-lethal blast injury, air embolism has been ignored, considered innocuous or believed to have not occurred. The high incidence of post-concussion syndrome (PCS), neurocognitive deficits, and mental health issues resulting from sub-lethal blast injuries in U.S. Iraq and Afghanistan War veterans has vexed military authorities and medical specialists. We propose that micro air embolism is a heretofore unappreciated etiologic factor.

MATERIALS AND METHODS

Materials and Methods: Using PubMed, PsychInfo, Google Scholar, Sci.gov, and PubCrawler, a systematic review of the literature was conducted identifying published papers in the following domains: biodynamics and physics of blast overpressure; primary blast injury; microbubbles in systemic circulation from diving and iatrogenic causes; neurological problems and microbubbles. When necessary, key documents were obtained from U.S. Government archives. Reference lists of articles were also scanned. Papers with both significant and null findings were included.

RESULTS

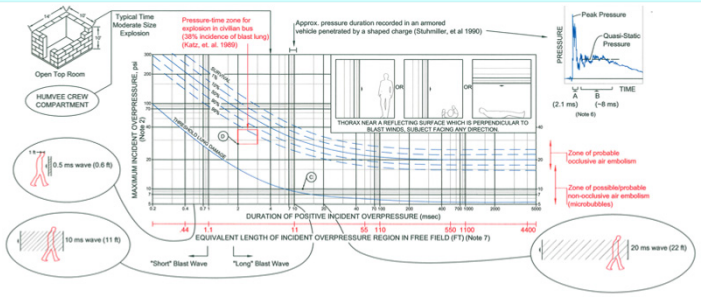
Blast-induced AE

- For mammals that die promptly from either air or underwater blast, air embolism has long been recognized as the primary cause of death (Desaga,1950; Shapnack, Johnson & Phillips, 1990; Richmond & Damon, 1991). Lung disruption is proportional to both magnitude and length of blast overpressurization (Buamoul, 2009) with disruption beginning to occur at modest overpressures easily within the range of pressures experienced by U.S. combat troops from improvised explosive devices (IED) (Fig 1 & 3).
- The disruption threshold is lowered by exposures near reflective surfaces, exposures inside structures that impede dispersion of the blast gases, and by longer exposure times. It is further lowered by repeat exposures in less than 24 hours (Stuhmiller, Phillips & Richmond, 1990).
- Benzinger (1950) concluded that because symptoms were only present when a blast hit the thorax, air embolism must originate in the thorax and becomes effective when it travels to the brain. Benzinger also found that small amounts of air in arterial circulation could readily reproduce neurologic symptoms seen in blast injury to dogs and humans. Only 1 cc of air injected into the pulmonary veins of a dog was sufficient to reproduce the electrocardiographic changes seen in blast-injured dogs (Phillips & Richmond, 1990).
- Maison (1971) outfitted a dog with a Doppler bubble detector on the carotid artery, exposed the dog to an LD50 air blast, and subsequently observed bursts of Doppler deflections going up the carotid correlating with respirations for approximately 30 minutes post-blast. The dog's carotid blood flow was observed to temporarily drop to near zero following each group of echoes, possibly indicating reduced blood velocity due to temporary distal occlusions (Fig. 2). The dog initially showed severe respiratory distress, but recovered. Postmortem exam showed evidence of residual lung hemorrhage, but no other damage. Maison concluded that the bubbles were "clinically silent".
- A conceptual model of how AE sequelae to blast exposure occurs, confirmed with rabbit model data, can be found in White (1971). Any fast-rising blast pressure wave long enough to produce significant chest compression is likely to produce some AE.
- Goh (2009) and Mayo & Kleger (2006) in separate articles regarding civilian blast casualty management advise that AE is a possible complication of exposure to air blast. However, neither author addresses the possibility of neurocognitive sequelae from AE.
- Protective vests reduced mortality & neural fiber degeneration in rats exposed to air blast (Long, et.al., 2009)

Evidence that microbubbles are NOT harmless

- Microbubbles were first recognized as a medical hazard in open-heart surgery decades ago (Barak & Katz 2005). Air emboli from various sources in the extracorporeal circulation (ECC) set and tubes can drift into the aorta and systemic circulation, carrying microbubbles to the brain. Clinical results of this unwanted event include major and minor neurologic injury, neurocognitive deterioration and an overall general decline in patient health (Barak, Nakhoul & Katz, 2008; Shaw et al., 1987). The degree of decline in cognitive performance has been correlated to the amount of air emboli delivered during the ECC (Deklunder et al., 1998[1,2]). Patients with neuropsychological deficits 5 to 7 days after coronary bypass graft surgery averaged nearly twice the number of emboli compared to those without deficits (Stump, et al., 1996).
- In mechanical heart valve carriers, bubbles are chronically delivered into the arterial system at variable rates, which can rise as high as 800 per hour in the cerebral circulation. Patients with these devices have been found to have impairment in episodic memory and deficits in working memory (Deklunder et al., 1998[1,2]).
- Multiple brain lesions in divers with no reported history of neurological DCS have been found to be strongly correlated with patent foramen ovale of high haemodynamic relevance. This finding lead the authors to a hypothesis that the brain lesions were the consequence of subclinical cerebral gas embolism (Knauth et al., 1997).
- A review of 140 cases of delayed DCS treatment (avg. delay 93.5 hrs) reported findings of neurocognitive symptoms including severely reduced executive function, apathy and antisocial behavior in 49% of the patients. 100% of the neurocognitive symptoms resolved with hyperbaric oxygen therapy. (HBOT) (Cianci & Slade, 2006).

Fig. 1: Blast Waves Are More Than Simple Shock Waves, Duration Makes a Difference



Notes to Fig. 1

1.Figure is based on the survival curves for a 70 kg man where the thorax is near a surface against which a blast wave reflects at normal incidence (Bowen, Fletcher, & Richmond,1968). data shown is for a single reflection where the total overpressure is ~2x incident pressure. Total pressures can be up to 8x incident pressure if circumstances are right (Richmond & Damon,1991). In free field exposures (no reflections) the damage thresholds are approx. 2x those shown. When used, free field pressure data values are plotted at 50% of actual.

2. "Short" and "Long" refer to the ratio of the length of the overpressure region to thorax dimensions. Long blast waves produce much greater chest compression (White et al., 1971).

3. Repeat exposures in less than 24 hours, lower the lung damage threshold (Stuhmiller, Phillips & Richmond 1990).

4.The lung damage threshold curve is based on an estimated damage threshold of 20% of the 50% mortality level (White et al., 1971). Recent data (Yang et al., 1996) suggests the threshold pressures for lung damage may be lower (circa 50%) than those shown.

5.Blast waveform is also important. However, that is beyond what can be addressed in this poster.

6.A = shock wave period, B= period where expanding blast gases maintain compartment pressure

7. Based on a wave speed of Mach 1. Most blast waves are faster (up to Mach 2+) increasing the wave length for the same time..

Fig. 2 Blood Velocity & Embolus Indications Following Canine Exposure to LD50 Air Blast

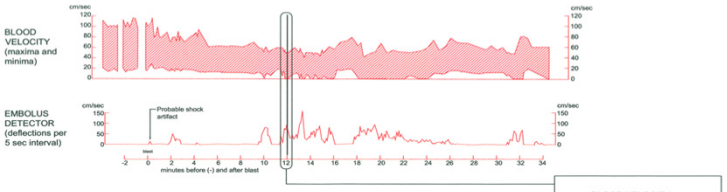
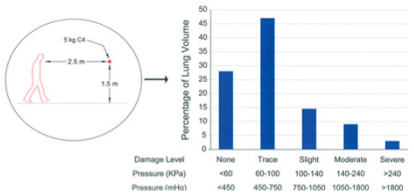


Fig. 3 . Lung Injury Prediction from CRDC Model



Notes to Fig 3.

1. Data shown are peak intro-thoracic pressures and lung damage estimates for a complex (2-peak) wave with a total impulse considered "threshold" for lung damage in a free field (Point D in Fig. 1)
2. Data from Yang, et.al (1996) suggests the threshold for "Trace" damage may be significantly lower that assumed by the CRDC model.

RESULTS (CON'D)

- In hemodialysis, CNS abnormalities attributed to microbubbles have been correlated with the duration of dialysis treatment. Barak & Katz (2008) attributed the abnormalities to microbubbles and stated "a small quantity of microbubbles may be clinically silent, while recurrent exposure has a slow, smoldering, chronic effect" (p. 2921)

Recent Combat Medical Literature

- Bauman et al. (2009) provides a summary of the test conditions and initial results from the PREVENT (Preventing Violent Explosive Neurotrauma) research program being conducted by DARPA. In the tests reported (swine model), the thorax and upper abdomen were protected to minimize the possibility of brain injury by indirect pathways. Some neurological damage was observed, and its significance is still being determined. However, the test conditions are of interest as they are also ones where lung injury can readily occur. Point C on Fig. 1 represents a typical Friedlander wave reported for the blast tube. Test set-ups were built to simulate exposures in the crew compartment of a Humvee with a blast under its floor and an open gunner port and in semi-confined space (open top room with dimensions as shown in Fig 1). In both cases the overpressure durations from a moderate sized charge were reported to be about 4 ms. The overpressure data was reported in general form only without numerical values. However, at 4 ms duration, the pressures required to produce lung injury are not large. In situations where the Humvee or building were to be fully closed, both the magnitude and duration of blast overpressures can be expected to be greater.
- Buamoul (2009) reports results from a computer model developed by Defence R & D Canada (CRDC) for estimating the blast damage to the lungs of sheep and humans. He reports the intra-thoracic pressure range currently accepted as the "threshold" for lung damage is 70 kPa (695 cmH20) to 110 kPa (1,091 cmH20), which corresponds roughly to the intra-thoracic pressures predicted by the model at exposures near the lung damage threshold line on the Bowen charts. The intra-thoracic pressures produced by even moderate size blasts can be very substantial (Fig. 3). They also vary widely with both time and location in the lung, suggesting that opportunities for localized AE may be plentiful. The model also indicates that complex (multi-peak) blast waves can produce higher lung pressures, and therefore greater risk of lung damage than do single peak, classic Friedlander waves of the same impulse value.
- **Recent work by Yang et al.,1996 (sheep model) suggests the lung damage threshold pressure may be as much as 75% lower than the Bowen charts (Fig 1) indicate when the threshold pressure is taken as the lowest pressure at which lung tissue damage is observable by light and/or electron microscopy.**

DISCUSSION

- It is well established that AE is a possible/probable sequelae of exposure to air blast.
- It is also well established that microbubbles are harmful to brains, and that symptoms may not manifest immediately.
- Blast overpressure exposures typical of the current wars in Iraq and Afghanistan, particularly blast exposures in confined spaces, are sufficient to create risk of lung damage. Quickly repeated exposures increase the risk.
- It is reasonable to expect that the degree of blast-related AE is a continuum ranging from no bubbles, to a few microbubbles to massive amounts depending on the exposure.
- The blast-related intra-thoracic pressures can be very substantial (Fig 3). The range customarily accepted as the threshold for lung injury is 7 to 11 times higher than the 80 mmHg (10.7 kPa) differential known to produce disruption of aveolar-capilary boundary tissues in slowly varying pressure environments such as diving (Neuman, 1997).
- Work by Yang, et. al (1996) suggests that lung tissue damage, and the concurrent possibility of transient microbubble release, can occur at lung damage levels insufficient to produce clinical blast lung and at overpressures substantially lower than indicated by the widely-used Bowen charts.
- The CRDC model confirms suggestions from prior efforts that complex blast waves typical of confined space exposures are more likely to be damaging to lungs than are the simpler waveforms typical of free-field blasts.
- Blast related bubble production, when it does occur, has been shown to be transient, lasting only 15 minutes to 3 hours for significant AE (Mayo & Kluger, 1996). The duration of microbubble production can be expected to be shorter still making them hard to detect.
- All recent publications that we found, including a recent review article (Cernak & Noble, 2009), were silent on the possible role of microbubbles as a mechanism for blast-related brain injury.
- When all the factors that may favor microbubble production are considered, it is difficult to expect they do not occur.
- Undetected arterial microbubbles have the potential to significantly confound research into other mechanisms of blast-related brain injury. **In research studies where there is a possibility of microbubble production, monitoring for their occurrence is recommended**.

The contribution of micro air embolism to blast-related brain injury may be significantly greater than has been previously believed.

SUMMARY/CONCLUSIONS

Available literature suggests that transient AE from primary blast exposure is possible, perhaps probable, at sub-lethal overpressures similar to the overpressures experienced by U.S. combat Veterans. Arterial microbubbles have been shown to be neurologically harmful and may contribute to the high incidence of post-concussion syndrome in blast injured veterans. Current research efforts are almost exclusively focused on the direct cerebral effects of blast waves. The AE pathway deserves prompt and thorough investigation.