# Diaphragmatic Cramp-like Spasm – A Novel Terminal Mechanism in Sudden Unexpected Deaths

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**Short Title:** Diaphragmatic Cramp in Sudden Death

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**Abbreviations: BDP**: bilateral diaphragmatic paralysis, **CK-MM**: creatine kinase isoenzyme (muscle type), **CNS**: central nervous system, **DCS**: diaphragmatic cramp-like spasm, **DD:** diaphragmatic dysfunction, **DF**: diaphragmatic flutter, **DP**: diaphragmatic paralysis, **RAMs**: respiratory accessory muscles, **REM**: rapid eye movement, **SIDS**: sudden infant death syndrome, **SUDC**: sudden unexplained death in childhood

*[Word Count: 301]*

**ABSTRACT**

**Background:** Diaphragmatic paralysis and diaphragmatic flutter are known to induce respiratory distress when sudden, bilateral and complete. Infants, who are most affected by unexpected sudden death and more reliant on diaphragmatic function for respiration, are unable to use accessory muscles sufficiently to compensate for acute diaphragmatic dysfunction. Autopsy studies in sudden infant death which systematically investigated diaphragmatic histology found significant abnormalities including contraction band necrosis in the majority.

**Hypothesis:** Non-cardiac, sudden unexpected death is primarily caused by "diaphragmatic cramp-like spasm" (DCS), a novel mechanism of respiratory arrest.

**Evidence supporting hypothesis:** Electrophysiologically and fluoroscopically documented case reports of patients with episodic bilateral diaphragmatic flutter or diaphragmatic myoclonus of high frequency (amounting to DCS) showed features of significant respiratory distress.

Autopsy studies of diaphragms in sudden infant deaths documented significant muscle necrosis and inflammation.

The negative intrathoracic pressures generated by inspiratory accessory muscles independent of a functioning diaphragm in DCS can explain the intrathoracic petechiae (Tardieu spots) and pulmonary edema commonly seen in sudden unexpected, non-cardiac deaths of all age groups. This is reminiscent of noncardiogenic pulmonary edema in living subjects.

REM-sleep inactivation of accessory muscles causes apnea in vulnerable infants with diaphragmatic fatigue, some requiring mechanical ventilation.

**Evidence against hypothesis**: Infants with diaphragmatic flutter did not have apneas or associated sudden deaths.

**Confirmation of hypothesis and implications:** This could be accomplished by electrophysiological detection of DCS in infants hospitalized for apnea. The same could be done at home for infants at high risk for sudden infant death syndrome. A creatine kinase level could screen for a recent history of cramps in infants with acute life-threatening events to select those for monitoring to detect, manage and prevent DCS. The patient's positive pressure, autoresuscitative rescue breath technique should be taught to all. Confirming chest rise with each rescue breath is an essential CPR priority.

*[Word Count: 2517]*

**Background:**

Bearhugs hurt. They can also be lethal when unable to expand the ribcage to breathe. These worrisome symptoms, when they occur spontaneously in the middle of night to a sleeping 7-year-old, are especially concerning.

The patient is a practicing male, 52-year-old medical doctor of Jewish ancestry. He recounted a history of breathing emergencies that awakened him from sleep sporadically throughout his childhood and youth, possibly longer (See *Patient's Perspective* in supplementary materials): Beginning at 7 years old alone in bed one night, he awakened gasping for air in a constricting, painful bearhug. He could not breathe in at all despite attempts at forced inspirations. There was no panic, rather he was baffled by the involuntary opening of his mouth at first. There was no history of panic attacks or other psychiatric disorders. No sleep problems or child abuse. The cramp-like rib pain was described as excruciating, constant in intensity and distributed in a C-shape under the nipple line radiating bilaterally from posterior-to-anterior with sternal sparing. He had the wherewithal to troubleshoot despite a growing sense of impending doom. Astonishingly, symptoms resolved immediately after learning by experimentation to partially exhale followed immediately by three short-burst, positive-pressure inspirations with pursed lips "like pilots breathe in a centrifuge". Upon repeated episodes over the years he recognized rib fasciculations to be prodromal and could be aborted with his rescue breaths.

Although our child patient was clearly not an infant at the time of symptoms, he had many risk factors overlapping with those in SIDS: male gender, history of gastroesophageal reflux and mild chronic diarrhea, residing in a colder climate, low birthweight, household cigarette smoke and deep sleeping with diaphoresis, prone positioning and a tendency to pull bed linens over shoulders and head.

We originally sought to find the cause for our patient's concerning nighttime symptoms. Clinical reasoning substantially reduced the list of differential diagnoses using key historical features: spontaneous nocturnal, recurrent, sudden on- and offset, cramp-like, bilateral rib (bearhug) pain with simultaneous inspiratory arrest (apnea). The diagnosis with highest likelihood was bilateral muscle cramps of the *intercostal muscles* and *diaphragm*, both respiratory (inspiratory) muscles. Thus, in generating the differential diagnosis, it inadvertently

led to a potentially novel mechanism of acute respiratory pump failure. One that is reversible given our patient survived.

Mammals have two vital pumps: the heart and diaphragm (**Fig. 1**). Yet the ratio of research papers on their potential involvement in sudden unexpected deaths is 250-to-1, respectively, predominantly in sudden infant death syndrome (SIDS). The diaphragm has essentially been ignored. Given respiratory arrest is possible with some diaphragm disorders it is important to realize some victims may not have lived to talk about it let alone be recruited into medical studies (survivorship bias). [1] As such, the full spectrum of patient presentations may be missed.

SIDS and sudden unexplained death in childhood (SUDC) are distinguished arbitrarily based on age (under and over 1 year, respectively). There is no evidence suggesting different causes, however, the incidence of SIDS is 38-times greater than SUDC. [2] Victims are typically found prone in bed and have congested, wet lungs at autopsy with intrathoracic petechial hemorrhages suggestive of asphyxia (Tardieu spots). [3,4,5] They are found in over 80% of SIDS and 50% of SUDC. [6,7] Based on their intrathoracic distribution, upper airway obstruction was first suggested by *Krous* (1984) and then by *Poets* (1999), however, there has been no concrete supporting evidence.

Diaphragmatic fatigue leading to respiratory pump failure in SIDS was proposed by *Siren and Siren* in 2011. [8] In their brilliant "critical diaphragmatic failure" hypothesis, they posited progressive *fatigue* terminating in diaphragm *failure* typically occurs from a non-lethal childhood infection superimposed on underdeveloped respiratory muscles as well as prone positioning and rapid eye movement-sleep inactivation of respiratory accessory muscles (RAMs) (**Fig. 2**). They later added contributions by hypomagnesemia, hyperthermia and tobacco smoke. If their hypothesis was true, however, one would expect a significantly higher SIDS incidence as these conditions are not uncommon in childhood. It is also missing a 'smoking gun' mechanism that precipitates diaphragmatic failure. In addition, progressive diaphragmatic fatigue would imply a period of several hours of respiratory distress leading up to sudden death, which is not observed in the majority of SIDS cases (however, could be subclinical).

**The hypothesis**:

Non-cardiac, sudden unexpected death is primarily caused by *novel* "diaphragmatic cramp-like spasm" (DCS).

**Explanation of hypothesis**:

Sudden cramping of a skeletal muscle renders it unable to perform work, effectively paralyzing it by contracture. In the case of the diaphragm, bilateral cramping should then lead to a state equivalent to bilateral diaphragmatic paralysis (BDP), a known disorder. In general, BDP is thought to terminate in *immediate* respiratory arrest when it is sudden, complete and occurs in those with weak RAMs. This appears to be the case in some young infants who are unable to support chest expansion by inspiratory RAM contractions. Syncope and death would occur within minutes, thus DCS is a terminal pathological mechanism.

Respiratory arrest by DCS has escaped detection because it is unpredictable, sudden, rapid, silent and mimics other conditions. Hypoxic syncope, for example, can masquerade as a seizure. As the diaphragm is an internal organ, abnormal contractions are not normally visible. Like ventricular fibrillation, a malignant terminal cardiac arrhythmia, pathological contractions do not persist postmortem making it difficult to confirm at autopsy.

With the onset of REM-sleep and consequent physiologic inactivation of most skeletal muscles including RAMs (primarily the external intercostal muscles), a sudden additional workload is placed on the diaphragm to maintain ventilation (respiratory load sharing). [9] This could catalyze diaphragmatic failure in vulnerable infants with diaphragm fatigue as proposed by *Siren*. [8, 10] We hereby add DCS *is* the pathological mechanism behind this process and suddenly culminates in a complete, bilateral, tetanic-like diaphragmatic cramp that is potentially fatal by Type II hypercapnic respiratory failure. Onset appears to involve abnormal diaphragmatic tone and neuromuscular hyperexcitability. [11] BDP and apnea ensue, not only in infants but also our 7-year-old patient. Fortunately, he was able to autoresuscitate.

In infants however, upon waking and physiologic reactivation of their underdeveloped RAMs in last-ditch attempts to inspire, such efforts would be futile without a functioning diaphragm. In fact, RAM contractions to breathe would be met with the combined resistance of pulmonary compliance and the tetanically contracted, paralyzed, immobilized diaphragm of DCS. This could be the mysterious airway obstruction suggested by *Krous* (and *Poets*). As negative intrathoracic pressures would build; the vacuum effect shunts systemic blood into the thorax, primarily the lungs, eventually rupturing capillaries from excessive hydrostatic pressures. This could form Tardieu petechiae and explain pulmonary congestion and edema also seen at autopsy

(**Figs. 3 & 4**). Finally, effective clamping of the inferior vena cava and possibly aorta by the hypercontracted diaphragm (by their apertures) would exacerbate the situation. (For the proposed sequence of events see **Table 1**). These findings are reminiscent of *noncardiogenic pulmonary edema* in living subjects.

Inspiratory respiratory muscle paralysis and paresis generally occur by pathologies affecting the CNS, phrenic nerve(s), diaphragm, RAMs or combinations thereof (**Table 2)**. Some are gradual in onset, unilateral and affect just the diaphragm such as phrenic nerve compression by a slow-growing tumour, whereas others are sudden, bilateral and involve both the diaphragm and RAMs. The latter includes certain electrocutions and neurotoxin poisonings like curare and *nicotine*, a known SIDS risk factor [12,13] Death by rapid respiratory arrest in nicotine ingestion occurs by prolonged paralysis of respiratory muscles (tetany). [14] Electrolyte disorders, acidosis and malnutrition contribute to diaphragm dysfunction, including fatigue, and may play a role in SIDS deaths as well as those in eating disorders. [15,16] Hypomagnesemia weakens respiratory muscles in children and is thought to increase muscle tonicity and excitability in SIDS. [17] Acidosis exacerbates this by increasing renal excretion of magnesium (and calcium). [18] Finally, hypercapnia has been shown to reduce diaphragmatic contractility. [19]

**Evidence supporting hypothesis:**

*Lopes* (1981) found REM-sleep inactivation of RAMs was associated with apnea in vulnerable infants with diaphragmatic fatigue, some requiring mechanical ventilation. [9]

Studies demonstrating immediate respiratory arrest and death in experimentally phrenectomized animals occurred predominantly in the very young (by removal of the phrenic nerve which innervates the diaphragm). [21] RAMs were still functional.

This is further supported by two reports of diaphragmatic paralysis induced by phrenic nerve injuries complicating pediatric cardiac surgeries. In the first, in four infants with new onset BDP, severe respiratory distress occurred repeatedly, some requiring repeat intubations despite functioning RAMs. [22] In the other, a retrospective study of 168 postoperative children with iatrogenic DP (both unilateral and bilateral), prolonged mechanical ventilation was needed in many. [23] *Smaller infants* and those with *BDP* had longer postoperative courses.

In adults requiring mechanical ventilation on an intensive care unit, 53% had diaphragmatic dysfunction (DD) on admission, as defined by twitch tracheal pressure in response to bilateral anterior magnetic phrenic nerve stimulation. [24] Mortality was higher in patients with DD — either on initiation of mechanical ventilation or during the subsequent ICU stay — compared to those who never developed DD (35 vs. 0%, $p = 0.04$).

A study of home-monitored SIDS victims by *Poets* (1999) showed that bradycardia, gasping and apnea occurred terminally. [25] Hypoxemic "ineffective gasps" were detected where inspiratory efforts were not followed by a rise in heart rate. This suggested hypoxemia was secondary to airway obstruction as opposed to central apnea.

Although laryngospasm, a known cause of airway obstruction, was proposed in SIDS using dogs, it did not cause respiratory failure or death. [26] Interestingly however, total cessation of diaphragmatic activity occurred temporarily in one animal whereas another had erratic diaphragm contractions.

Histological signs consistent with DCS at autopsy: *Kariks* (1989) reported focal areas of acute, anoxic muscle fiber coagulative necrosis in 198/242 (82%) SIDS victims' diaphragms. [27] "Contracture (contraction) bands", the presence of which indicated recent origin of irreversible cell injury, were also found (**Fig. 5**). They are produced by an extreme compaction of sarcomeres. [28] Such findings reflected, "lethal diaphragmatic damage had occurred *terminally* under hypoxic conditions and from a *hypercontractile state*". Inflammation and fibrous scars were also found in near-miss SIDS cases.

Tobacco smoke exposure is a well-known SIDS risk factor, yet its mechanism remains unknown. High nicotine levels were found in the lungs of SIDS victims compared to controls. [29] Earlier, in *Franke and Thomas'* 1936 review on 70 childhood nicotine poisonings, they were "convinced death was due to *peripheral paralysis* of respiratory muscles". [30] It is therefore plausible infants exposed to nocturnal tobacco smoke (while sleeping in an *upstairs, heated* bedroom) are at risk for diaphragmatic failure by DCS. Nicotine might lower its cramp threshold. [10]

Viral respiratory tract infections are known to influence risk factors for abnormal diaphragmatic contractility including acidosis and hypercapnia. [32]

**Evidence against hypothesis:**

Neonates with diaphragmatic flutter (DF) up to 300/min are still able to simultaneously breathe normally. The flutter is obvious on clinical examination but in four resulted in gradual evolution of respiratory distress requiring continuous positive airway pressure support in two and mechanical ventilation in one. [33,34] Apnea was not observed. Cardiopulmonary resuscitation was not required and the deterioration in respiratory effort was not fast.

In another case series of three infants between 1 and 20 weeks old with restricted lung function due to bronchopulmonary dysplasia and hospitalized because of respiratory syncytial virus bronchiolitis, DF with a frequency of 150 to 350/min was detected on a combination of inductive plethysmography, electrocardiography, pulse oximetry and impedance pneumography. [35] During brief periods of DF there were no falls in oxygen saturation or heart rate and apneas were not present. The respiratory rate during DF did not differ from the rate immediately preceding flutter. None of these infants subsequently suffered from SIDS.

A reason why the above examples cited against our hypothesis may not be applicable to what we propose is that DF might be at the *milder end* of the spectrum of diaphragmatic dysfunction, whereas DCS could be at the *severe end*. This is where flutter is thought to merge into a high amplitude, almost continuous contraction series (tetany). What really counters our hypothesis, however, is the fact patients known to have suffered recurrent DF did not die from this condition to our knowledge.

**Confirmation of hypothesis:**

To confirm our hypothesis, investigations need to identify DCS as a cause of respiratory distress. In infants hospitalized for apnea or acute life-threatening events, this could be achieved by electrophysiological monitoring of the diaphragm (by inductive plethysmography, electrocardiography, pulse oximetry and impedance pneumography). It could also include surface diaphragm electromyography as well as bedside ultrasound or fluoroscopy to detect abnormal diaphragm contractions upon apneic events. The same could be used for older children

and adults presenting with sudden or episodic respiratory distress. In such patients, a serum creatine kinase isoenzyme muscle-type (CK-MM) level would be helpful in retrospectively determining the presence of muscle spasms. CK-MM is released by skeletal muscle during a cramp and would be expected to be elevated in DCS.

A detailed analysis of the time course of CK levels after an isolated calf muscle (gastrocnemius) cramp was performed in a 48-year-old man. [36] It revealed on a baseline CK level of 117 IU/L, this adult, after suffering a severe cramp at 0200 am which lasted several minutes associated with muscle aching, was found to be 299 IU/L six hours later. A day later, it rose to a peak of 534 IU/L and remained elevated at 334 IU/L for 48 hours. The level normalized after five days.

On the basis of this finding, the age group with the highest incidence of life-threatening apneas — infants less than 2 months old — could be investigated by CK-MM levels after apneas or other life-threatening events. This could be compared to age-matched controls. An elevated CK-MM could then trigger the aforementioned investigations to detect diaphragm dysfunction. Such investigations could also use a four-channel pneumocardiogram. [37] It was found successful in the detection of DF. [38]

Given marked diaphragmatic abnormalities exist in SIDS at autopsy (contraction band necrosis, myositis and scarring), this needs to be further explored and could form the basis for the development of diaphragm biomarkers [26]. Additionally, autopsies in sudden unexpected deaths should assess diaphragm histology. [39,40]

**Implications of a confirmed hypothesis:**

Had our 7-year-old patient not autoresuscitated reportedly by exhaling followed immediately by three positive-pressure inspirations to overcome DCS, he likely would have perished ultimately to be diagnosed with SUDC. Such deaths could be prevented by teaching his rescue technique to all children capable of understanding.

In another patient, DF initially stopped for three months with passive insufflation of the lungs by a patient-controlled manual resuscitator. [41] Due to recurrences, it was later replaced by a portable non-invasive ventilator. It reduced the frequency of episodes by providing diaphragmatic rest. This could be helpful in cases at high risk for DF/DCS.

Finally, if DCS is confirmed, parents and other caregivers will need to be taught to look for chest rise with each CPR rescue breath.

## TABLES AND IMAGES

**Table 1 – Hypothetical Sequence of Diaphragmatic Cramp-like Spasm/Respiratory Arrest.** The DCS mechanism has not been experimentally validated. This is a hypothetical example of an otherwise healthy infant sleeping alone in a crib at night in winter in a smoking household. Heart rate, oxygen saturation and breathing movements (but not respirations) are being wirelessly monitored by a typical, commercially available home SIDS device.

1. Progressive diaphragmatic fatigue from a mild upper respiratory infection combined with prone sleeping in an *upstairs*, *heated* bedroom with household cigarette smoke.
2. Also had low-grade fevers and partially formed stools in past 24 hours. Along with heavy blankets and rebreathing of exhaled gases, these culminate in mild dehydration, mild hyperthermia, mild-to-moderate metabolic acidosis, moderate hypercapnia, mild hypoxia and mild hypomagnesemia. Along with prone positioning and nicotine absorption, all contribute to diaphragm dysfunction and neuromuscular hyperexcitability.
3. Physiologic respiratory accessory muscle (RAM) recruitment secondary to diaphragm fatigue, primarily the intercostal muscles. Observed as rib retractions.
4. Falls asleep. Physiologic REM-sleep inactivation of RAMs by CNS. Adds a sudden workload to the fatigued diaphragm and pushes it past cramp threshold. Precipitates DCS which effectively paralyzes the diaphragm, inducing inspiratory arrest (apnea). Oxygen saturations begin to slowly drop yet insufficient to trigger alarm.
5. Immediately wakes in a painful bearhug from the cramped diaphragm. RAMs reactivated. Unable to cry out because of inability to inspire. Ineffective gasping. No alarm as chest movements continue with each breathing attempt.
6. CNS signaling to the untrained, underdeveloped RAMs (normal in infancy) to contract to expand the ribcage in dire struggle to inspire. Met with combined resistance of pulmonary compliance and the hypercontracted, immobilized diaphragm. Similar to breathing against a 100% upper airway obstruction, RAM contractions build negative intrathoracic pressures (yet insufficient to expand lungs). The vacuum effect draws systemic blood into intrathoracic organs, primarily the lungs. Elevated hydrostatic pressures rupture capillaries, forming Tardieu petechiae. Exacerbated by *effective clamping* of inferior vena cava by the hypercontracted diaphragm (aorta too possibly). Infant loses consciousness and RAMs weaken from hypoxia.
7. Hypoxia, bradycardia or lack of body movements finally trigger the alarm but only 3-5 minutes remain before cardiac arrest.
8. Cyanotic, unresponsive child found by panicked parents who call 911 and initiate CPR. Chest compressions started. Mouth-to-mouth rescue breaths attempted but met with

airway resistance from both improper neck positioning and the hypercontracted, immobilized diaphragm. Parents not trained to look for chest rise (to confirm adequate rescue breaths).

9. Chest compressions resumed but the primary respiratory issue remains unaddressed.
10. Rescue breaths done hurriedly and again without confirmation. Panic and ineffective care continue.
11. Cardiac arrest.
12. Intrathoracic Tardieu petechiae, pulmonary congestion and edema found at autopsy. Diaphragm histology notable for contraction band necrosis in some segments along with inflammation and fibrous scars.

**Table 2 – Etiologies of Inspiratory Respiratory Muscle Paralysis and Paresis**. The CNS, phrenic nerve(s), diaphragm and/or RAM may be involved and can be combined. Insults can be sudden or gradual, unilateral or bilateral and complete or incomplete. Loss of neuromuscular function is *complete* in paralysis and *partial* in paresis (weakness).

| | | Onset | Side | RAM Involvement |
|---|---|---|---|---|
| **Multi-organ (CNS, phrenic nerve(s), diaphragm, respiratory accessory muscles)** | | | | |
| Electrocution | Lightning, low- and high-voltage shocks | S | Both | ✓ |
| Neurotoxin | Nicotine, botulism, tetanus, curare, organophosphates, carbamates, tetrodotoxin, strychnine, envenomations | S | B | ✓ |
| Medication | Neuromuscular blockers, aminoglycosides | S | B | ✓ |
| Electrolyte | Hypomagnesemia, hypocalcemia, low and high potassium, hypophosphatemia | S,G | B | ✓ |
| Metabolic | Acidosis *(DKA)* , endocrinopathies (*pheochromocytoma crisis), eating disorders* | S,G | B | ✓ |
| Inflammatory | Vasculitis, pneumonia, pleurisy, herpes zoster, SARS-CoV-2 (COVID-19) | G | B | ✓ |
| Neuropathic & myopathic | Guillain-Barré syndrome, polio, ALS, myasthenia gravis, Lyme disease, rabies, muscular dystrophy, polymyositis, dermatomyositis, inclusion body myositis | G | B | ✓ |
| **Phrenic Nerve** | | | | |
| Traumatic | Cervical spinal cord transection (above C5) | S | B | ✓ |
| | Cervical soft tissue injuries (blunt, penetrating, traction, compression) | S | U | 0 |
| Iatrogenic | Birth trauma (asphyxia), chiropractic manipulations | S | Both | 0 |
| | Cardiothoracic surgeries, cardiac cryoablation | S | Both | 0 |
| Compression | Cervical osteoarthritis, tumours (bronchogenic, mediastinal), aortic aneurysm | G | U | 0 |
| **Diaphragm** | | | | |
| Traumatic | High-velocity: contusion, hemorrhage, rupture | S | Both | 0 |
| | Low-velocity: *winding injury* (celiac or solar plexus syndrome) | S | Both | 0 |
| Exposures | *Cold water submersion, conducted electrical devices (Taser, stun gun)* | S | B | 0 |
| Spontaneous | *Diaphragmatic cramp-like spasm* | S | B | 0 |

RAM: respiratory accessory muscle, S: sudden, G: gradual, Both: bilateral and unilateral, B: bilateral, U: unilateral,
CNS: central nervous system, DKA: diabetic ketoacidosis, ALS: amyotrophic lateral sclerosis, *Italics:* putative (unproven).

**Figure 1 – Diaphragm and Thorax.** Anatomical location of the respiratory diaphragm in relation to the heart, lungs and abdomen. The diaphragm is a dome-shaped skeletal muscle with a large central tendon (not shown). It is the primary muscle of respiration. When it normally contracts, it descends into the abdominal cavity and creates negative intrathoracic pressure to expand the lungs passively.

*Courtesy of https://www.scientificanimations.com, CC BY-SA 4.0, Wikimedia Commons 2020. Labels added by Gebien.*

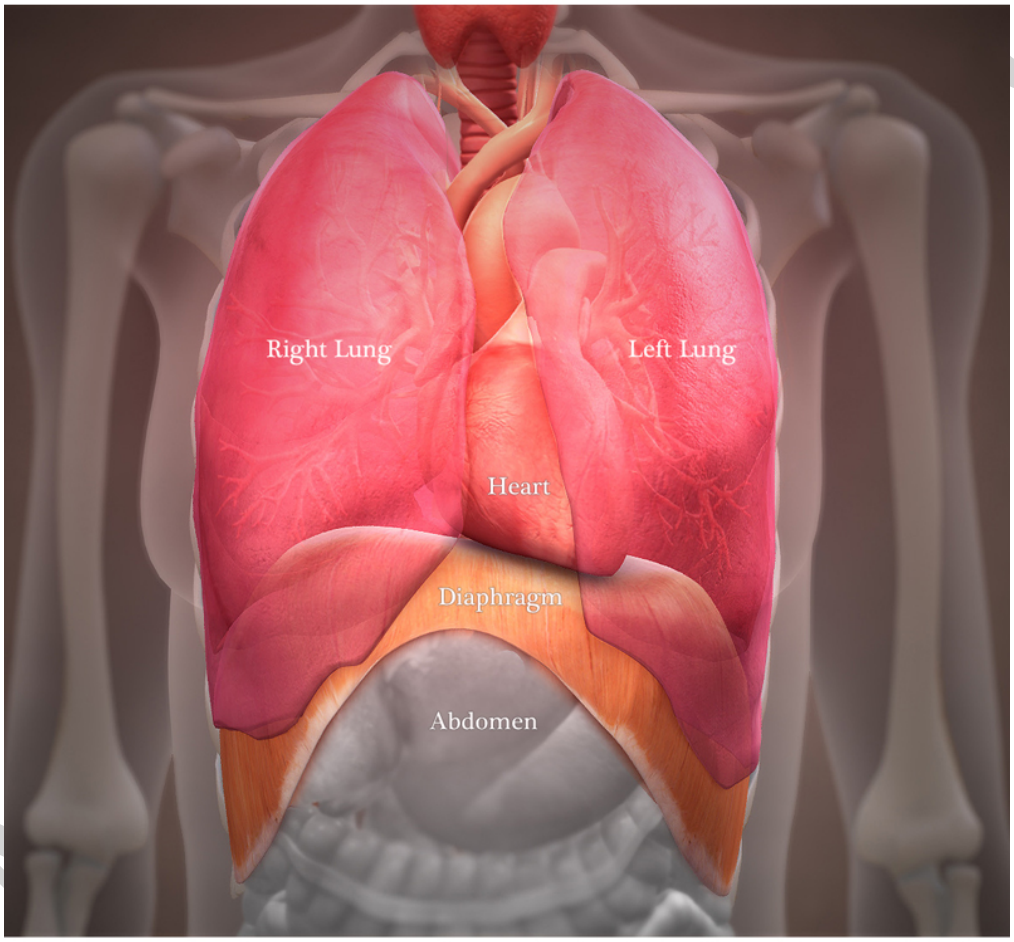


**Figure 2 – Muscles of Respiration.** The primary inspiratory muscles are the diaphragm and paired left and right external intercostal muscles (ICMs, lavender). The latter reduce diaphragmatic workload in adults by their bucket handle movements which widen the ribcage. Theoretically, if the ICMs were to suddenly fail, apnea would not occur as long as the diaphragm continued functioning. Contrarily however, if the diaphragm suddenly and completely failed, apnea and respiratory arrest could.

*With permission by www.concept2.co.uk/training/breathing.php.*

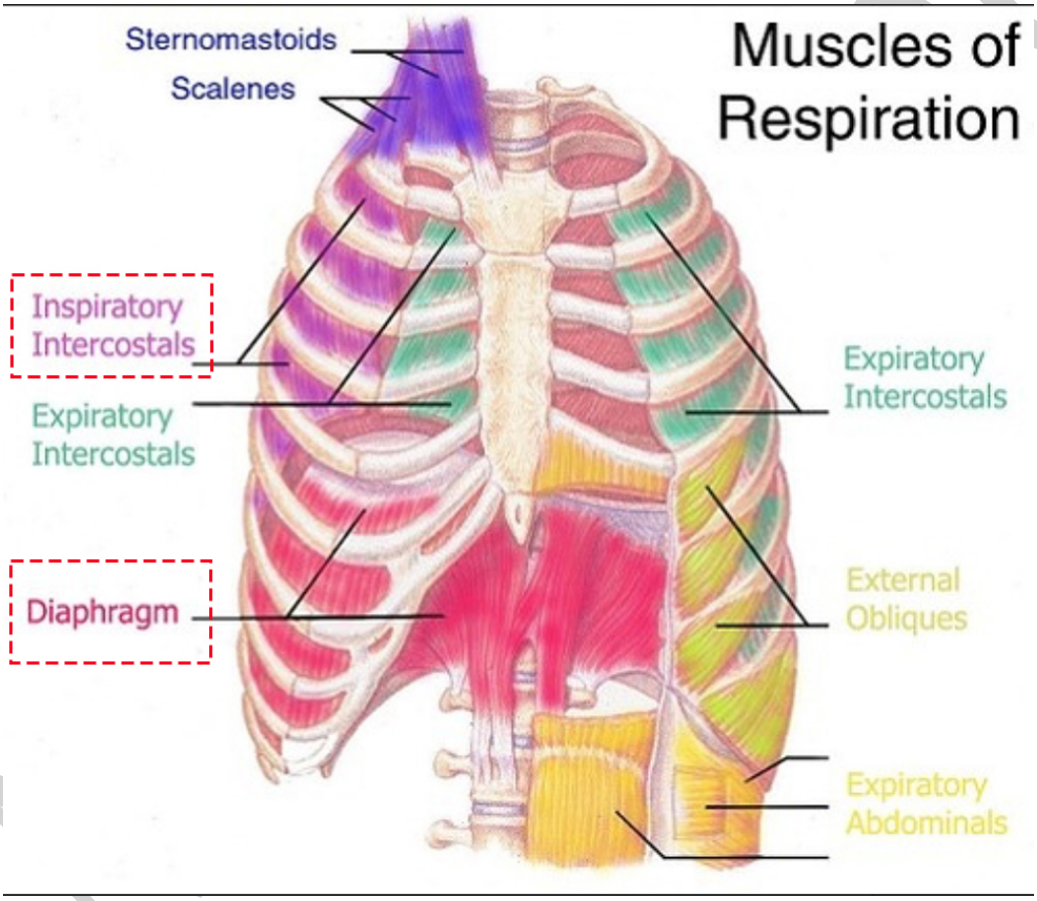
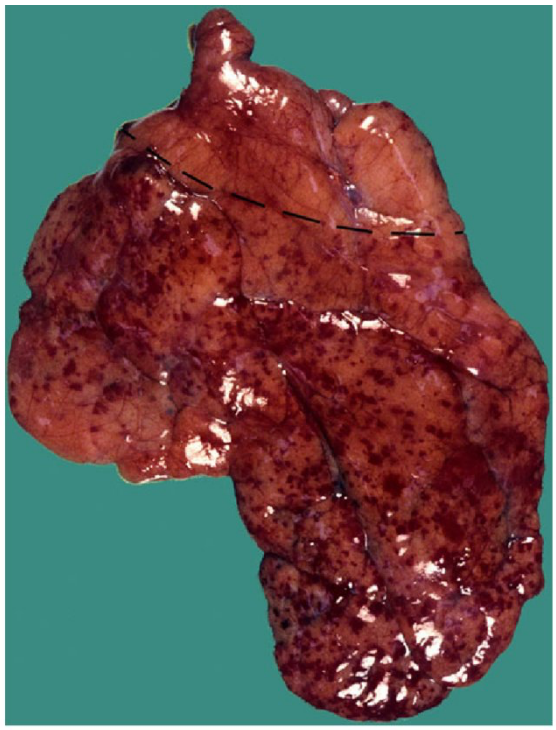


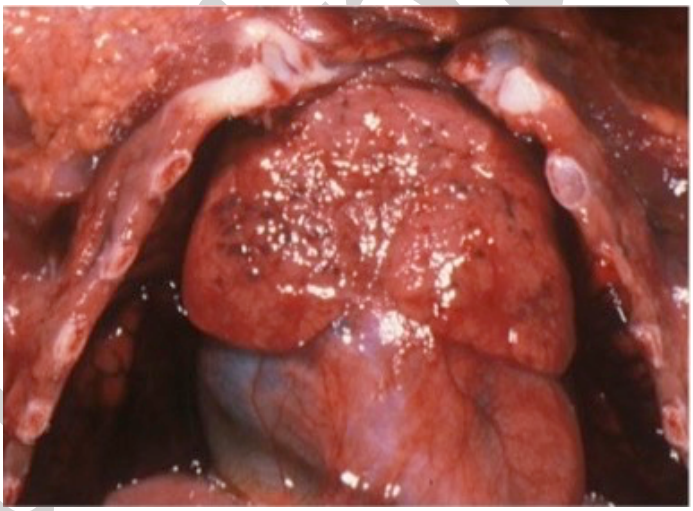
**Figure 3 – Thymus Gland in Asphyxia. A)** Beckwith's sign. The inferior, larger portion of the thymus is anatomically situated within the thoracic cavity whereas the smaller, superior segment is not (interrupted line). Sharp increase in the number of Tardieu petechial hemorrhages in the intrathoracic segment. **B)** Neonatal thymus (atop the heart) with Tardieu petechiae.

**A)**



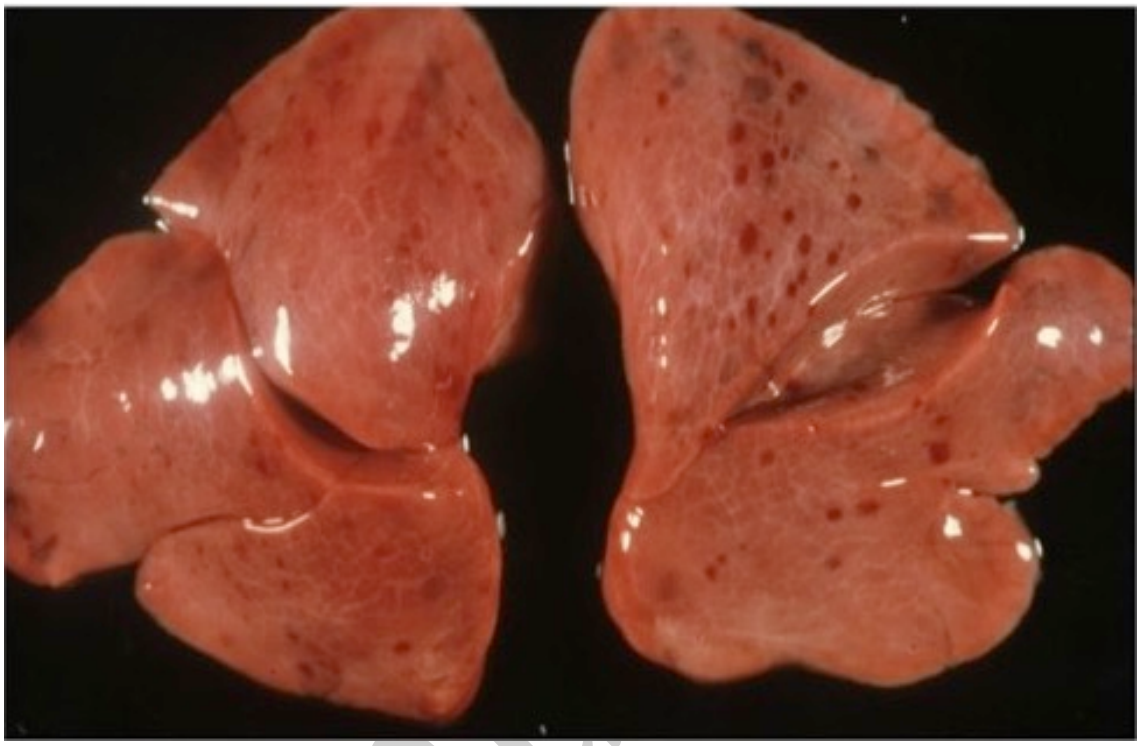
*Courtesy of Prof. Roger W. Byard.*
*In "Sudden Death in the Young", 3rd Ed.*
*Cambridge Univ. Press © 2010.*

**B)**



*Courtesy of Dr. Robert Benton MD.*
*ObstetricalPathology.com, 2023.*

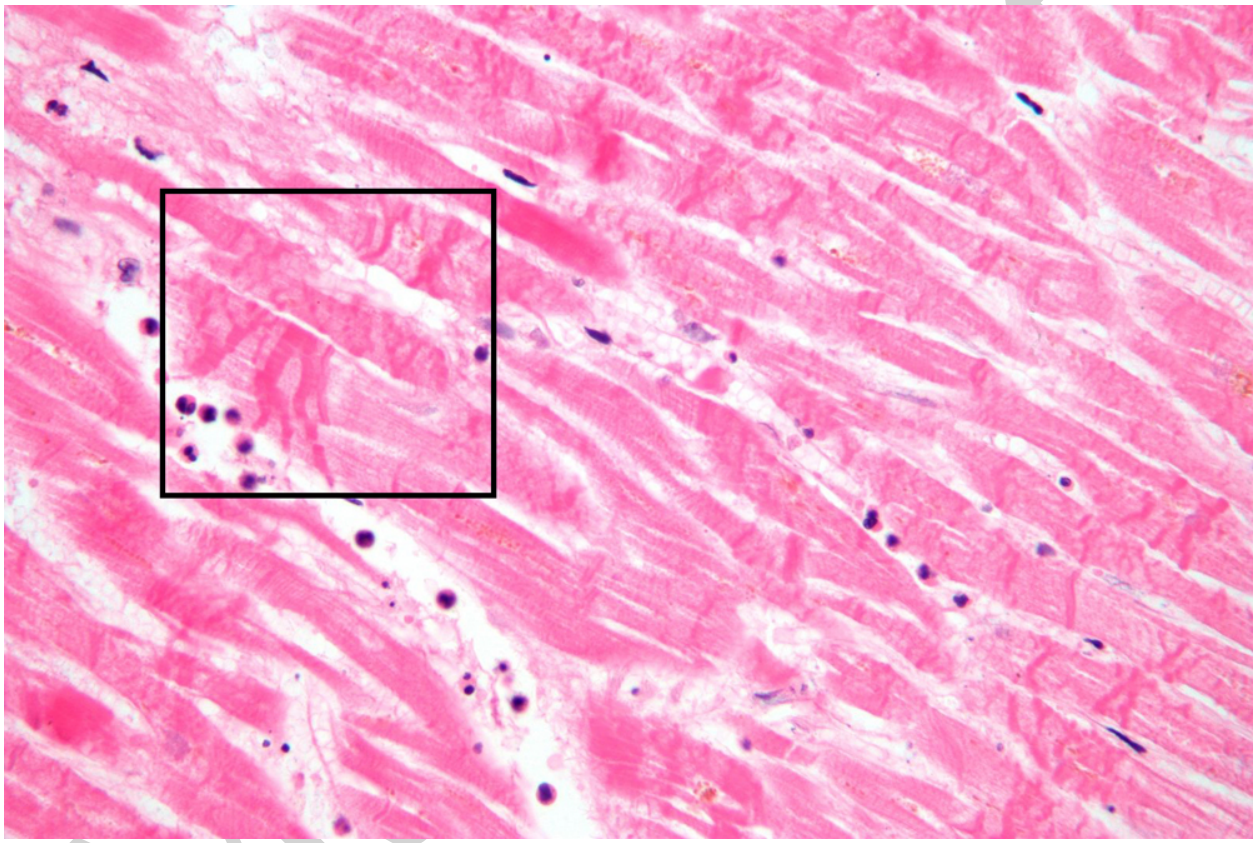
**Figure 4 – Fetal Asphyxic Lungs with Tardieu Spots.** Postmortem intrathoracic, subpleural petechial hemorrhages are indicative of suddenly generated, terminally negative intrathoracic pressures.



*With our respect and gratitude. Courtesy of Dr. Robert Benton MD. From ObstetricalPathology.com, 2023.*

**Figure 5 – Contraction Band Necrosis.** High magnification micrograph of cardiac myocytes oriented longitudinally. Contraction band necrosis appears as intensely eosinophilic (dark pink) thick bands spanning the width of the sarcoplasm (box outline). Indicative of acute anoxic sarcomere hypercontraction and rupture. A similar process occurs in the majority of diaphragms in SIDS victims.

*Courtesy of 'Nephron', CC BY-SA 3.0. Wikimedia Commons, 2009.*



## SUPPLEMENTARY MATERIALS

*Patient's Perspective*

The patient account is written by a practicing medical doctor of Jewish ancestry born in 1970 (52 years old). After receiving trauma counselling in late 2022 he recalled in great detail life-threatening breathing emergencies that had awakened him from sleep sporadically throughout his childhood and youth. He feels he came within a breath of losing his life each time. It appears his memories were repressed as a survival (defense) mechanism. Notably, he had multiple childhood risk factors overlapping with those identified in SIDS.

> "One night while alone in bed at 7 or 8 years old, I suddenly awoke from an excruciating, cramp-like pain in my ribs that felt like someone had picked me up from behind in a tight bearhug. The pain radiated to the front in a C-shaped distribution with sternal sparing. I couldn't breathe in at all and was also baffled because my mouth had opened involuntarily at first as I gasped for air. This all happened in under three seconds. As I fully awoke, turning to tell "the person who was bear-hugging me to stop", I was shocked to realize I was in my bed and that nobody was there. The bearhug and inability to breathe (apnea) persisted.
>
> Despite the growing sense of impending doom, I began to troubleshoot by experimentation. When I tried inhaling more forcefully it was met with equal and opposite, *complete resistance* to airflow. It was futile. My next test, to exhale, was successful though and I remember telling myself not to lose all the air in my lungs so to conserve it. I still couldn't breathe in and the pain continued. I did not have stridor, choking, fullness or a foreign body sensation in my throat and no palpitations or chest discomfort.
>
> What I did next was lifesaving.
>
> I tried something new by partially exhaling followed immediately by three short-burst inhalations with pursed lips to increase the inspiratory pressure. To my relief, the pain and apnea resolved completely. Crisis averted, so I went back to sleep *as only a seven-year-old can* despite a near-death experience. Soon afterwards I noticed a pilot on TV spinning in a centrifuge used the same distinctive, pursed lip breathing technique. I had never seen that before.
>
> The following morning I was puzzled because the pain had all but disappeared. I had already learned from prior ankle sprains, severe pain like that typically lasted days if not longer.

The breathing emergencies recurred sporadically throughout my childhood and youth but only at night while fast asleep. I do not know if I had any associated illnesses, however, it's interesting I frequently had mild diarrhea with most bowel movements (which also continued throughout my childhood and youth undiagnosed).

Eventually I recognized, in my sleep, prodromal flickering pains (fasciculations) in my ribs to be a warning sign of the impending bearhug pain and inspiratory arrest like that of the first episode. I would wake from this and use my rescue breaths (RBs) to abort the full-fledged attack. I can say with certainty the fasciculations and pain felt like that of a *limb* muscle cramp. I should also note the full bearhug pain came on *just at the very end of expiration* (and could be aborted by quickly breathing in). I can still recall how it always spread from a spot in my right posterolateral ribs to the encircling, painful bearhug in a millisecond.

The RBs were so loud and high-pitched I remember awakening one night to their sound. It appears I had grown so accustomed *I did them in my sleep*. Oddly, I also recall telling myself that night to 'keep it quieter next time' because I didn't want to wake anybody else up. My memory of that particular bedroom places it in our family's newer house, therefore, between ages 17 and 23. I'm not certain if I had any further episodes after that.

There are a few notable childhood medical conditions to share.

Due to severe gastroesophageal reflux, malnourishment and failure to thrive over my first year of life I underwent an uncomplicated, open exploratory-laparotomy with Nissen fundoplication at 18-months of age. It confirmed and definitively treated a congenital hiatal hernia. I recovered well, quickly gained weight and do not recall ever having reflux.

Since age 8 or 9 years, I frequently experience painful fasciculations and muscle cramps that cause contracture-like stiffness in the affected limb. One day the small muscles of the hand are affected (claw hand), whereas the next involves larger ones such as a calf or posterior thigh. With repeated episodes over the years, fasciculations alert me to abort the full intensity cramp by quickly stretching the affected muscle. I have not received a diagnosis for this ongoing condition.

In addition, beginning at roughly 10 years old, I occasionally become suddenly and extremely fatigued during prolonged, intense exercise. I soon learned it occurred when not eating properly beforehand. Carbohydrate-rich foods prevented and aborted symptoms.

Social history: I am the second male child of a Gravida 4, Para 2 smoker. Brother denies sleep-related pain and nocturnal breathing problems. I slept alone in an upstairs bedroom. Notably, I had stopped thumb-sucking around the same age as the onset of the breathing emergencies (important because pacifiers are known to be SIDS protective).

In terms of risk factors overlapping with SIDS, mine were numerous including male sex, low birthweight, reflux, chronic diarrhea, residing in a colder climate, household cigarette

smoke from maternal use, nocturnal diaphoresis, deep sleeping with preference for the prone position and tendency to pull bed linens over my shoulders and head.

I do not have a history of panic attacks, anxiety, depression or sleep disorders such as obstructive sleep apnea, night terrors or sleep paralysis. No cardiac abnormalities such as palpitations, exercise intolerance or syncope. No respiratory issues such as bronchospasm, pneumonia, choking episodes or prolonged cough or colds. No allergies, anaphylaxis or unusual childhood infections. No history of seizure, atypical headaches or focal muscle weakness. No family history of cardiac arrhythmias or sudden unexpected deaths including SIDS.

* * *

*I survived these life-threatening events because as opposed to an infant, I had the benefit of wherewithal and muscle coordination possessed by an older child. It is only now upon reflection as an adult do I realize how lucky I am to be alive.*

*I am determined to eradicate DCS.*

***Sleeping children need our help…<u>now</u>."***

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