Pathophysiology of inner ear decompression sickness: potential role of the persistent foramen ovale

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Abstract

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Inner ear decompression sickness (inner ear DCS) may occur in isolation ('pure' inner ear DCS), or as part of a multisystem DCS presentation. Symptoms may develop during decompression from deep, mixed-gas dives or after surfacing from recreational air dives. Modelling of inner-ear inert gas kinetics suggests that onset during decompression results from supersaturation of the inner-ear tissue and in-situ bubble formation. This supersaturation may be augmented by inert gas counterdiffusion following helium to nitrogen gas switches, but such switches are unlikely, of themselves, to precipitate inner-ear DCS. Presentations after surfacing from air dives are frequently the 'pure' form of inner ear DCS with short symptom latency following dives to moderate depth, and the vestibular end organ appears more vulnerable than is the cochlea. A large right-to-left shunt (usually a persistent foramen ovale) is found in a disproportionate number of cases, suggesting that shunted venous gas emboli (VGE) cause injury to the inner ear. However, this seems an incomplete explanation for the relationship between inner-ear DCS and right-to-left shunt. The brain must concomitantly be exposed to larger numbers of VGE, yet inner ear DCS frequently occurs in the absence of cerebral symptoms. This may be explained by slower inert gas washout in the inner ear than in the brain. Thus, there is a window after surfacing within which VGE arriving in the inner ear (but not the brain) would grow due to inward diffusion of supersaturated inert gas. A similar difference in gas kinetics may explain the different susceptibilities of cochlear and vestibular tissue within the inner ear itself. The cochlea has greater perfusion and a smaller tissue volume, implying faster inert gas washout. It may be susceptible to injury by incoming arterial bubbles for a shorter time after surfacing than the vestibular organ.

Key words

Diving; decompression illness; inner ear; right-to-left shunt; patent foramen ovale (PFO); persistent foramen ovale; review article

Introduction

Decompression sickness (DCS) is caused by bubble formation from dissolved inert gas during or early after ascent from a compressed gas dive.[1] These bubbles may form if the sum of dissolved gas pressures in a tissue or its microcirculation exceeds ambient pressure (a state referred to as 'supersaturation').[2] Decompressions from pressures as low as 1.35 ATA (3.5 m depth) have resulted in detection of venous gas emboli (VGE).[1] Bubble formation in blood and/or tissues may occur sub-clinically but, depending on factors that are presumed to include their size, number and location, these bubbles may produce mild to serious symptoms reflecting involvement of one to many organ systems.[3] Inner ear involvement in DCS may manifest as vestibular symptoms and signs (vertigo, nausea, vomiting, ataxia) or cochlear symptoms (deafness, tinnitus) or both.[4] Vestibular manifestations are the commoner.[4,5] Inner ear involvement may be part of a multi-system presentation, but inner-ear DCS may also occur as an isolated or 'pure' event.

Early case series of inner-ear DCS associated the injury with deep mixed gas diving, and commonly symptoms arose during decompression (that is, whilst the diver was still ascending).[6] Not surprisingly, inner-ear DCS has been reported to occur during decompression from deep technical dives.[7] Although pure inner-ear DCS was originally associated with mixed gas diving, it has since become clear that this injury may follow typical recreational dives using air though, as will be discussed, these dives are usually in the deeper range of air diving.[5] In these cases, symptoms typically develop within the first hour of surfacing. Several case series have demonstrated an unexpectedly high proportion of inner-ear DCS cases are subsequently demonstrated to have a large persistent (patent) foramen ovale (PFO).[4,8–10] This article does not purport to be a systematic review of all relevant literature and, therefore, we do not describe a search methodology. However, these authors have maintained a strong focus on this particular form of DCS since 2002, and this article refers to those publications that we believe are key to characterising and explaining its presentation and pathophysiology.

Inner-ear DCS during decompression from deep dives

As mentioned above, a subset of inner-ear DCS cases occurs during decompression from deep dives whilst the diver is still immersed and completing the stops prescribed by their decompression algorithm. The onset of vertigo and intractable vomiting during immersion presents obvious hazards and a challenging 'Catch 22'. Thus, if a vertiginous, vomiting diver remains underwater there is a possibility of an

airway accident leading to drowning. However, if the diver omits significant periods of decompression by surfacing not only may the inner-ear DCS symptoms worsen, but the inevitable excessive supersaturation in other tissues may also provoke life-threatening, multi-organ DCS.

Not surprisingly, inner-ear DCS and its avoidance is of significant interest to deep technical divers. Their dives typically involve the use of 'mixed gases' containing helium for its low density and non-narcotic properties, with 'gas switches' to mixes containing less helium, more nitrogen and more oxygen at shallower decompression stops.[11] These switches are made in the belief that they accelerate decompression and to save money on the cost of helium. Prevalent anecdotes arising from commercial and military deep, bounce-diving programmes in the 1970s and 1980s temporally related the onset of inner-ear DCS symptoms to these gas switches in a noticeable proportion of cases.[6] This fostered a widespread belief that inner-ear DCS was, at least in some cases, caused by an inert-gas counterdiffusion phenomenon following such switches.

Counterdiffusion of inert gases as a cause of bubble formation in the skin and inner ear was investigated in the 1970s after pruritus and vestibular symptoms were seen when humans breathing (and surrounded by) an oxygen-helium chamber atmosphere were switched to breathing gas mixes containing nitrogen or neon.[12,13] In explanation, the inward diffusion of helium across the skin (towards blood and tissue containing less dissolved helium) was assumed to be faster than diffusion of nitrogen towards the chamber atmosphere in the opposite direction, and this was assumed to cause inert gas supersaturation and bubble formation in the skin, with consequent development of pruritus. This process was referred to as "*isobaric gas counterdiffusion*" given that it occurred without any change in the chamber pressure itself.[13]

It was much less obvious why bubbles would form in the vestibular organ under the same experimental conditions because, with the possible exception of the middle ear, there was no obvious source of exogenous helium that would exchange with nitrogen in blood across the inner ear to cause inner ear supersaturation in a manner analogous to the skin. Indeed, authors of much of the related work acknowledged that provided a diver was not surrounded by helium, a switch from breathing a helium-based mix to breathing a nitrogen-based mix should produce a transient (and advantageous) under-saturation in body tissues because helium was predicted to diffuse more quickly from tissue to blood than nitrogen would diffuse from blood to tissue.[13]

This issue received a contemporary re-evaluation with the 2003 publication of a kinetic model to predict inert gas partial pressures in three compartments representing the membranous labyrinth, perilymph and endolymph of the inner ear.[7] It is important to appreciate that the membranous labyrinth is the site of the functionally important receptors of the cochlea and vestibular end organs, and it is the only one of the three compartments that is perfused. The model was used to predict the effect of an isobaric helium-to-nitrogen breathing gas switch which produced vestibular symptoms in the chamber experiments discussed above.[13] This revealed a fascinating consequence of the unique anatomy of the inner ear in which the perilymph and endolymph are non-perfused compartments that take up and eliminate inert gas through the perfused membranous labyrinth. After a period of heliox breathing, the perilymph, in particular, accumulates a substantial reservoir of helium. Following a switch to nitrox breathing, owing to a higher diffusivity of helium than of nitrogen, diffusion of helium from the perilymph and endolymph to the membranous labyrinth exceeds the diffusion of nitrogen in the opposite direction. At the same time, owing to higher solubility of nitrogen than of helium in blood, delivery of nitrogen to the membranous labyrinth in the arterial blood exceeds the removal of helium in the venous outflow. Together these could cause a transient supersaturation of the membranous labyrinth without decompression.

With respect to the Lambertsen and Idicula experiment, in which vertigo occurred after a switch from breathing heliox to breathing a mixture of oxygen, helium and 10 ATA (1.01 mPa) of nitrogen at an absolute pressure of 37.4 ATA (3.79 mPa),[13] the model predicted isobaric supersaturation of 0.4 ATA (40 kPa) which exceeded previously reported thresholds for bubble formation in vivo,[14] and this was, therefore, a plausible explanation for the vestibular symptoms reported in that study. In this regard, the perilymph/endolymph 'helium reservoir' can be seen as acting in an analogous (albeit transient) role to the helium chamber atmosphere in the experiments which caused skin symptoms.

The model was developed primarily in an attempt to explain pure inner-ear DCS arising during decompression from deep, mixed-gas technical dives, and the modelling of one such event (a decompression dive to 110 metres' sea water (msw) for 25 minutes) showed that even prior to any gas switches the membranous labyrinth had become substantially supersaturated (1.7 ATA, 172 kPa peak) during the ascent.[7] Thus, one explanation for the onset of inner-ear DCS during decompression from deep dives was simply that the inner ear was allowed to become excessively supersaturated, which could provoke bubble formation in situ. In this case report, the helium-to-nitrogen gas switch resulted in a much smaller effect on membranous labyrinth supersaturation than in the Lambertsen experiment, mainly because the partial pressure of nitrogen substituted for helium was comparatively small.[7] Indeed, the counterdiffusion effect was manifest only as a transient slowing of membranous labyrinth gas washout.

We suspect that the isobaric counterdiffusion effects of typical gas switches in technical diving would rarely, if

Table 1
Numbers of inner-ear DCS cases presenting with isolated inner ear symptoms and within the latency categories specified in those series reporting compatible data; only one diver (in the Ignatescu study[8]) developed symptoms during ascent
* % out of 211; † combined numbers and % for latency >30 min

Study	*n*	'Pure' inner ear DCS	Latency of symptoms after surfacing (min)		
			0–30	31–60	>60
Ignatescu[8]	33	16	22	7	3
Klingmann[4]	34	28	20	9	5
Nachum[5]	29	15	18	6	5
Smerz[18]	28	Unknown	21	3	4
Gempp[9]	115	98	98	17†	
Totals (%)	239	157 (74)*	179 (75)	59 (25 †)	

Table 2
Numbers of inner-ear DCS cases presenting with vestibular only, cochlear only and combined presentations in those series reporting compatible data

Study	*n*	Vestibular	Cochlea	Vestibular and cochlear
Klingmann[5]	34	19	0	15
Nachum[4]	29	10	4	15
Smerz[18]	28	19	0	9
Gempp[9]	115	88	7	20
Totals (%)	206	136 (66)	11 (5)	59 (29)

Table 3
Methods and outcomes of testing for right-to-left shunt (RLS) in inner-ear DCS cases from those series reporting compatible data; all four studies used bubble contrast; TTE – transthoracic echocardiology; TCD – transcranial Doppler; * % out of 179

Study	*n*	Test	RLS +ve	Large RLS
Ignatescu[8]	30	TTE	24	24
Klingmann[4]	34	TCD	25	Not specified
Cantais[10]	34	TCD	28	24
Gempp[9]	115	TCD	95	89
Totals (%)	213		172 (81)	137 (77*)

ever, be sufficient to produce inner-ear bubble formation in their own right, and inner-ear DCS occurring during decompression from deep, mixed-gas dives may be explained primarily by inadequate decompression. However, if a switch takes place when there is substantial pre-existing supersaturation of the membranous labyrinth, it is plausible that the resulting counter-diffusion effect could transiently augment this supersaturation and increase the probability of symptomatic bubble formation. In this regard, it is germane to mention that the basis for using nitrogen switches to accelerate decompression from helium dives has recently been challenged,[15] and in the absence of gas cost as a factor (e.g., when using a rebreather), the advantages of performing gas switches are now open to substantial debate.

Finally, for completeness, we cannot exclude the possibility that the right-to-left shunt of VGE, for instance across a PFO, as discussed below, might be relevant to isobaric inner-ear DCS and in some inner-ear DCS cases arising during decompression, because VGE formation occurs both during isobaric counterdiffusion of helium and nitrogen across the skin and during decompression.[16,17]

Inner ear DCS arising after diving

The second subset of inner-ear DCS cases arises after diving. There are now five substantial series of inner-ear DCS cases (Table 1).[4,5,8,9,18] For completeness, we note that two other series[19,20] were considered but not included in this review because of case overlap with Klingmann (2012).[4] Of the total 239 divers presented, only one developed symptoms during decompression.The vast majority arose after air diving to moderate depths. Pooled maximum depth data for the incident dives in the 96 cases from three of the series show a median maximum depth of 34.5 msw (range 15–122 msw).[4,5,8] Neither of the other two series[9,18] reported individual dive depths to allow data pooling but the mean depth maxima in these series were 32 msw and 41 msw respectively. Many cases (74.4% in series reporting relevant data) exhibited 'pure' inner-ear symptoms (that is, there were no other DCS manifestations) and in most cases these symptoms developed with relatively short latency; 85.4% presented within 60 minutes of surfacing. The proportion of divers presenting with inner-ear symptoms classified as vestibular only, cochlear only, or both vestibular and cochlear are shown in Table 2 for those series with compatible data. The vestibular organ appears affected both more often and more often in isolation than the cochlear organ. In summary, inner-ear DCS occurring after surfacing can be characterised as a frequently isolated or 'pure' clinical syndrome with short symptom latency following dives to moderate depths, and to which the vestibular end-organ appears more vulnerable than the cochlea.

A striking feature of inner-ear DCS occurring after surfacing is strong association with the presence of a right-to-left shunt. Data from relevant studies are summarised in Table 3.[4,8–10] Three studies used transcranial Doppler (TCD) (or occasionally carotid Doppler) to detect a right-to-left shunt after injection of bubble contrast solution into a peripheral vein.[4,9,10] These tests can detect shunting but do not delineate the anatomical source of the shunt, though it was presumed in most cases to be via a PFO in a study using transthoracic echocardiography with bubble contrast.[8] Studies of right-to-left shunt (or specifically PFO) in control groups of divers who have not reported DCS, find an approximately 25% incidence of any right-to-left shunt and a 12% incidence of

large right-to-left shunt (where 'large' is usually defined as spontaneous shunting of bubble contrast).[10,21] Comparison of these values to those reported for the case series in Table 3 suggests that right-to-left shunt (and particularly large shunts) are significantly over-represented amongst divers suffering inner-ear DCS. A similar, although somewhat weaker association exists between right-to-left shunt and cerebral, spinal and cutaneous DCS.[22–25]

The most obvious interpretation of the association between right-to-left shunt and some forms of DCS is that a shunt allows VGE to bypass the pulmonary capillaries which normally act as a filter and prevent most VGE from reaching the arterial circulation.[26] Arterialised bubbles then impact organs where they cause harm. This pathophysiological mechanism requires that VGE occur at or before the time of symptom onset and that arterialised bubbles have sufficient lifetimes to reach the affected organ; both of these conditions are plausible for inner-ear DCS. To accommodate the typically short symptom latencies for inner-ear DCS (Table 1), VGE must form very early after surfacing from recreational air dives. Indeed, VGE are commonly detected less than 30 minutes, and as soon as two minutes, after decompression from no-stop chamber dives.[27]

There is a paucity of related data following recreational dives in the field, because many relevant studies do not begin VGE monitoring within the first 30 minutes after surfacing, and those that do frequently report the peak bubble count or grade over multiple sequential observations without providing data for each observation. Nevertheless, one study showed that 26% and 45% of unrestricted first and repetitive (respectively) recreational scuba air dives resulted in Spencer VGE Grades 2–4 around 30 minutes post dive.[28] The unsurprising finding in the same study that dives with a higher predicted probability of DCS produced more VGE may explain the moderately deep (and, therefore, provocative) nature of most incident dives in the inner-ear DCS series cited here. There is ample evidence that even small arterialised VGE are able to reach the cerebral circulation. For instance, TCD detection of arterialised agitated saline (in which air bubbles are of similar size[29] to decompression VGE[30]) has demonstrated this on many occasions (Table 3).

Thus, the intuitively obvious relevance of a right-to-left shunt is that small VGE that become 'arterialised' across the shunt could embolize the inner ear vascular supply and produce vestibulo-cochlear dysfunction. A clinical observation that lends circumstantial weight to this hypothesis is the occasional onset of symptoms in temporal relation to lifting or straining early after surfacing;[8] such manoeuvres would be expected to increase right heart pressures and promote flow across a right-to-left shunt. However, the commonality of the blood supply to both inner ear and the brain, another 'at-risk' organ, raises questions about the provenance of this relatively simple explanation.

The arterial supply to the inner ear is a branch of either the basilar artery or the anterior inferior cerebellar artery (itself a branch of the basilar artery) and flow through these cerebral vessels is vastly greater than through the labyrinthine artery. Since tiny bubbles will tend to distribute with flow,[31] the posterior circulation of the brain will be exposed to a substantially greater proportion of any arterialised VGE passing up the basilar artery. Despite this, inner-ear DCS commonly occurs in the absence of any symptoms of other organ involvement (Table 1) begging the question "*how can there be only inner-ear manifestations when the brain must simultaneously be exposed to much greater numbers of emboli*"?

It could be argued that the inner ear represents a functionally important and sensitive end-arterial territory that might be particularly vulnerable to injury by arterial micro-bubbles. However, the brain also contains functionally important end-arterial loci.[32] Moreover, there are other clinical situations in which patients are exposed to many small arterial bubbles but in which it is the brain that appears more vulnerable to injury than the inner ear. A contextually relevant example is the introduction of microbubbles to the arterial circulation in a strongly positive PFO test using bubble contrast. These bubbles are of similar size to VGE produced in decompression,[29,30] and they occasionally produce symptoms suggestive of evanescent cerebral injury,[21,33–35] but there are no reports of inner-ear injury following PFO tests. Similarly, microbubbles may contribute to post-operative cognitive impairment following cardiac surgery,[36] but (to our knowledge) peri-operative exposure to these bubbles has never been associated with inner-ear injury.

An explanation for the almost paradoxical selective vulnerability of the inner-ear to injury by arterial microbubbles after diving was first proposed by the present authors.[37] Using published models for predicting inert gas tensions in brain and inner ear, comparison was made of supersaturation in the membranous labyrinth and brain over the first hour after surfacing from a no-decompression-limit air dive to 30 msw.[7,15,38] This depth corresponded to the typical depth of incident dives in inner-ear DCS series reported at that time. The models predicted nitrogen wash out from the brain and inner ear with approximate half times of 1.2 and 8.8 minutes respectively. Consequently, on the simulated dive where ascent was conducted at the prescribed rate, the brain would develop a small and transient supersaturation whereas the inner ear would become significantly supersaturated during ascent, and this would decay over approximately 30 minutes after surfacing.[37]

We proposed that any small arterial bubbles arriving in the inner ear during this 'supersaturation window' would tend to grow from inward diffusion of supersaturated gas (as has been demonstrated in other tissues)[39] whereas similar bubbles entering the brain microcirculation would not grow, and would tend to redistribute through to the venous side.

On this basis, bubbles arriving in the inner ear early after a dive could be expected to produce greater harm. However, notwithstanding its rapid inert gas elimination kinetics and consequent resilience in comparison to the inner ear, it is plausible that the brain can still be injured by large numbers of small arterial bubbles, as is believed the case in cardiac surgery.[36] This would explain the previously reported over-representation of large right-to-left shunts among divers suffering cerebral DCS.[22]

Two recent studies extended our hypothesis to an explanation for the apparent vulnerability of the vestibular apparatus in comparison to the cochlea.[4,8] The authors cited data demonstrating that blood flow to the cochlea exceeds blood flow to vestibular organ by a factor up to times four,[40,41] and that cochlea tissue volume is smaller than that of the vestibular organ.[42] These characteristics would result in a shorter perfusion half-time for inert gas exchange in the cochlea than in the vestibular organ. Thus, the greater susceptibility of the vestibular organ than the cochlea to injury (Table 2) may be explained by slower gas washout and, therefore, more prolonged supersaturation in the vestibular organ than in the cochlea. As a result there will be a longer period during which bubbles can grow in the vestibular organ than in the cochlea.

Thus, in summary, it seems plausible that a large PFO predisposes to inner ear DCS by allowing VGE to enter the arterial circulation. This is more likely to occur following dives which are more provocative for VGE formation, and right-to-left shunting of VGE may be promoted by lifting, straining, or exercising early after diving. In respect of inner-ear DCS, shunting of VGE is maximally hazardous early after a dive when the inner ear remains supersaturated with inert gas. Although not investigated formally, it is plausible that a similar mechanism involving residual tissue supersaturation may explain the unexpectedly high prevalence of RLS among divers suffering spinal and cutaneous DCS. Shunted VGE are less likely to injure the brain because it eliminates inert gas very quickly. However, cerebral symptoms could occur if large numbers of VGE are shunted.

The implications of these pathophysiological mechanisms to treatment of relevant DCS cases and to decision making around investigation and management of right-to-left shunts after a relevant DCS episode are beyond the scope of this summary, and are considered in other papers in this issue.

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