Review articles

Immersion pulmonary oedema: a cardiological perspective

Peter T Wilmshurst

Royal Stoke University Hospital, Stoke-on-Trent, ST4 6QG, United Kingdom
peter.wilmshurst@tiscali.co.uk

Key words
Cold; Exercise; Hypertension; Rebreathers; Renal artery stenosis; Takotsubu cardiomyopathy; Transpulmonary pressure; Case reports

Abstract

(Wilmshurst PT. Immersion pulmonary oedema: a cardiological perspective. Diving and Hyperbaric Medicine. 2019 March 31;49(1):30–40. doi: 10.28920/dhm49.1.30-40. PMID: 30856665.)
It is postulated that immersion pulmonary oedema (IPE) occurs because of combinations of factors that each increase the hydrostatic pressure gradient between the pulmonary capillaries and the alveoli. The factors, by definition, include the effects of immersion, particularly raised central blood volume and hence cardiac filling pressures. Breathing against a negative pressure is important but the magnitude of the effect depends on the relation of the diver's lung centroid to the source of the breathing gas and the breathing characteristics of diving equipment. Other factors are cold-induced vasoconstriction, exertion and emotional stress, but variations of the responses of individuals to these stimuli are important. Hypertension is the most frequent cardiovascular disease predisposing to IPE but other medical conditions are implicated in some patients.

Background

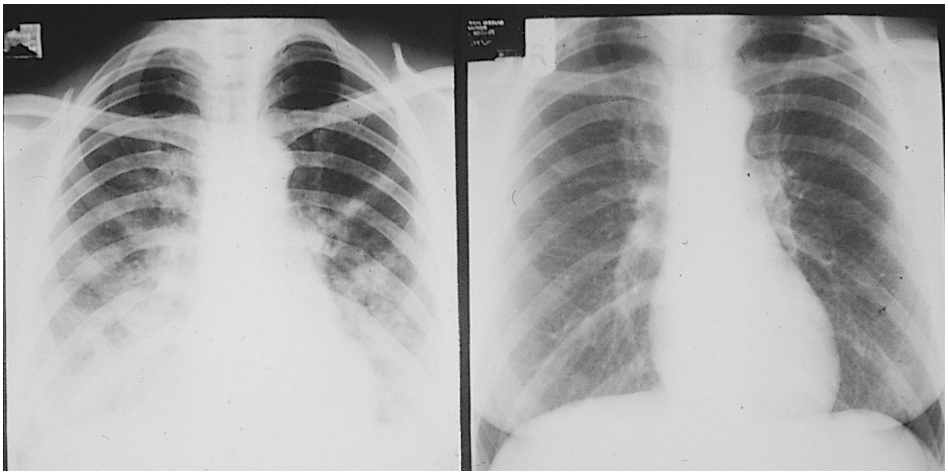
Immersion pulmonary oedema (IPE) occurs in divers and surface swimmers and onset is acute.[1] Acute pulmonary oedema can occur if the pulmonary capillary permeability is increased as a result of damage to the alveolar-capillary interface (non-cardiogenic pulmonary oedema).[1] Cardiogenic pulmonary oedema occurs without increased capillary permeability when the hydrostatic pressure gradient across the pulmonary capillary membrane exceeds the oncotic pressure – the osmotic pressure exerted by plasma proteins.[2] The term cardiogenic pulmonary oedema implies that the cause is within the heart, but that is not always so. If the plasma albumin concentration is low, so that the plasma oncotic pressure is also low, pulmonary oedema can occur when the hydrostatic pressure gradient across the pulmonary capillary membrane is within the normal range. The distinction between cardiogenic and non-cardiogenic pulmonary oedema is not always sharp. Cardiac disease with high pulmonary capillary pressures can cause fracture of capillaries to produce bloodstained oedema and haemoptysis, so the oedema is not a pure transudate. The evidence suggests that IPE is a form of cardiogenic (or hydrostatic) pulmonary oedema.

The precise hydrostatic capillary pressure equivalence of the oncotic pressure depends on the plasma concentrations of proteins, particularly albumin, but in normal individuals it is approximately 25 mmHg.[2] At rest, healthy individuals have a lower pulmonary capillary pressure (less than 12 mmHg) and there is net movement of water from the alveoli into the pulmonary capillaries. Even in normal individuals the difference between dry lungs and onset of pulmonary oedema formation may be an increase in pulmonary capillary pressure of only 15 or 20 mmHg.

An illustration of the delicacy of the balance between pulmonary oedema and dry lungs is the common appearance of a chest X-ray (CXR) of a patient with pulmonary oedema (Figure 1a). There is airspace opacification at the lung bases but clearer lung apices. That is because, in a patient who is upright, the pulmonary capillaries situated at the level of the left atrium will have a capillary pressure that mirrors left atrial pressure, but pulmonary capillaries that are 15 cm above the level of the left atrium will have a capillary pressure that is 15 cm water (H_2O) pressure (approximately 11 mmHg) less than left atrial pressure. Cardiogenic pulmonary oedema forms most rapidly when the pressure gradient across the pulmonary capillary membrane increases rapidly to a high level to cause 'flash' pulmonary oedema.[3]

In most situations, acute pulmonary oedema occurs because of a significant increase in left atrial pressure: plasma protein concentrations do not fall rapidly and usually intra-alveolar pressure changes are small. However, acute pulmonary oedema can occur when there is sudden extrathoracic airway obstruction, such as glottic obstruction following extubation after general anaesthesia, resulting in a patient exerting high negative inspiratory pressures – effectively sucking fluid from plasma into the alveoli.[4] Slower onset of pulmonary oedema is described in dogs when resistance to inspiration caused a 15–20 cm H_2O negative pressure during inspiration that was maintained for 20 to 120 minutes (min).[5] More chronic pulmonary oedema is described in man when there

Figure 1
The left chest X-ray is of the first diver recognised as having pulmonary oedema triggered by diving; the right chest X-ray is of the same diver four weeks later



were comparably negative airway pressures maintained for days.[6]

Cardiogenic pulmonary oedema is produced in the opposite ways to the therapeutic methods employed to clear it from the lungs, which are by reducing pulmonary capillary pressure (with diuretics and vasodilators) and by increasing intra-alveolar pressure, for example by use of continuous positive airway pressure (CPAP).[7]

Anyone, no matter how fit they are, can develop pulmonary oedema if the pressure gradient across their pulmonary capillary membrane is increased sufficiently for long enough. The data and clinical observations suggest that a number of factors that individually increase the pressure gradient across the pulmonary capillary membrane can, when acting in combination, produce a cumulative increase in the pressure gradient to cause IPE.

Immersion pulmonary oedema

In 1977, I was in the boat that picked up a pair of divers from my diving club in the United Kingdom (UK). They had aborted a dive to 20 m in water at 8°C after 5 min because one had become severely breathless for no apparent reason. She was cyanosed and coughing up blood and froth.[8] I examined her. She had a tachycardia, gallop rhythm and basal crepitations. Hospital investigations, including a CXR six hours after she left the water, confirmed pulmonary oedema (Figure 1a). By the time the CXR was taken she was already feeling better and she refused treatment. A repeat CXR four weeks later was normal (Figure 1b); an electrocardiogram (ECG), echocardiogram, exercise test and myocardial perfusion scan were also normal. She said that she had had six previous episodes. Years later she was found to have hypertension and subsequently she had an episode of high altitude pulmonary oedema.[9]

In the next two years I saw two other divers in my club who had IPE. Both described two episodes. One had been so hypoxic that he became unconscious for 10 min. All episodes occurred when diving in relatively cold UK conditions. Each of the three divers had dived in warmer waters without having any problems. These three divers were the subjects of the initial report of "*recurrent pulmonary oedema when scuba diving*".[10]

It appeared that there was an individual susceptibility to IPE, because some individuals were affected repeatedly when their dive buddies were unaffected. Also there were extrinsic factors because only immersion triggered their pulmonary oedema. The occurrence of IPE in three divers in a club with approximately 200 members suggested that this previously unrecognised condition might be common.

A presentation in 1984 included cases that we thought had died from "*heart failure when diving*" and concluded that "*it is probably a very serious and frequent cause of illness amongst divers…and an occasional cause of death*".[8]

VASCULAR RESPONSE TO COLD

Eleven divers out of a larger group of patients with IPE agreed to be subjects of a research study.[1] Their ages were 38 to 60 years (mean 45.6 years). They had no detectable cardiac disease and had good exercise capacity on land. They each had many years of diving before their first episodes, suggesting that susceptibility developed with time or age. Episodes occurred when diving in cooler British waters but some had dived in warmer waters without symptoms. The equipment they had used during the episodes included single- and twin-hose demand valves. Two also had pulmonary oedema when surface swimming. The vascular responses to cold (head and neck packed in towels soaked in ice-cold water) and to a raised partial pressure of oxygen

(67%) in the supine position in these eleven divers were compared with ten control divers. The stimuli induced pathological vasoconstriction in the divers that had a history of IPE compared with the controls. In a previous report, an initial group of IPE sufferers had increased venous tone and reduced venous compliance at rest and with vasoconstrictor stimuli.[11] (Comparable data were available for the whole group, but the *Lancet* requested that the paper be shortened and those data removed.)

An important observation was that nine of the eleven developed evidence of cardiac decompensation during the physiological stimuli out of the water, including one who had frank pulmonary oedema and required treatment with an intravenous vasodilator infusion.[1] None of the controls had evidence of cardiac failure. During follow up for an average of eight years the majority of the divers with IPE developed hypertension. It was postulated that increased vascular reactivity to cold in some individuals combined with the increased preload that occurs during immersion might be enough to trigger pulmonary oedema when immersed.[12] It is notable that hyper-reactivity during a cold pressor test in children is predictive of development of hypertension during follow up for 45 years.[13]

The observation in the Lancet paper that those who had IPE were at increased risk of having pulmonary oedema when out of the water was supported by the report of three individuals without evidence of heart disease who had pulmonary oedema when scuba diving but also had pulmonary oedema unrelated to immersion.[9] One had three episodes of pulmonary oedema precipitated by emotional stress. One had three episodes precipitated by sexual intercourse. The third, an exceptionally fit member of special forces, had an episode during strenuous exertion in a cold climate. Others have reported that hypertension is associated with IPE and with recurrent episodes of IPE.[14,15]

The increased preload caused by immersion combined with cold-induced vasoconstriction does not explain all cases of IPE. In a report of four individuals who had radiologically confirmed pulmonary oedema when scuba diving and/or swimming and another with probable IPE based on history without radiological or clinical confirmation, the vascular responses to cold were compared to six controls.[16] No differences were found between the groups and none developed evidence of cardiac decompensation during the experiment. The protocol used was similar but not identical to the protocol in the earlier study.[1,16]

With the exception of a woman aged 39 years, who had hypertension, the individuals reported were much younger (23–27 years)[16] than the age range (38–60 years) of subjects reported previously,[1] and none had hypertension. The woman aged 39 had five episodes of IPE (two were when diving in water colder than 6°C, and three were when swimming long distances in competition or training in water warmer than 18°C). The three younger individuals had one episode of IPE each. Two occurred when diving in cold water (less than 6°C). The other occurred during a competitive long-distance swim in warmer water (20.6°C). Recreational scuba diving and competitive open water swimming each involve immersion, but generally the latter involves considerably more exertion during immersion.

EXERCISE

Further evidence appeared that there is another younger group of patients who get IPE .[17,18] Eight out of 30 male military recruits (aged 18–19 years) developed pulmonary oedema during a 2.4 km swimming time trial in seawater at 23°C.[17] They swam in a supine position using fins. The recruits each drank five litres of water during the two hours before the swim. Two of the eight had recurrence of IPE when they repeated the swim without prior fluid loading. This suggests that when immersed some individuals are at increased risk of developing IPE when there is only one additional factor increasing the gradient across the pulmonary capillary membrane (i.e., exercise) whilst others needed a further additive factor (i.e., fluid loading).

The same group later reported a further 70 fit male military recruits age 18–19 who had IPE during a three-year period and 16 of these had recurrent episodes.[18] The episodes represented 1.8% of all swimming trials performed. The authors postulated factors predisposing to IPE in fit young men including increased pulmonary vascular pressures from cold and exercise plus "*during head-out immersion, negative pressure respiration due to the hydrostatic pressure differences between upper and lower airways produces transmural pulmonary hydrostatic forces that favor a fluid shift from pulmonary vasculature to the alveoli*." Obviously the pulmonary vascular pressure that is important in formation of pulmonary oedema is pulmonary capillary pressure. When pulmonary capillary pressure is elevated, pulmonary arterial pressure is often increased secondary to the backpressure transmitted from the left heart via the pulmonary capillaries. However, when pulmonary artery pressure is increased without an increase in pulmonary capillary pressure by pathology proximal to the pulmonary capillaries, such as in primary pulmonary hypertension or massive pulmonary embolism, pulmonary oedema does not occur. Others have also suggested a role of negative pressure breathing in aetiology.[19]

Support for the possibility of two subgroups of people having IPE comes from Duke University. In one study, 36 divers with IPE were reported and another 292 cases identified from the published literature.[20] In recreational divers and swimmers with IPE the mean age was 47.8 $\pm$ 11.3 years and, within military divers and swimmers, mean age was 23.3 $\pm$ 6.4 years. Hypertension was the most frequent risk factor documented, particularly in recreational divers and swimmers who had IPE.

The same group compared 10 subjects with a history of IPE and 20 controls. They had radial artery and pulmonary artery catheters inserted before exercising on a cycle ergometer while submerged in water at 20°C.[21] The IPE group had significantly greater pulmonary artery pressure, pulmonary capillary wedge pressure, systemic vascular resistance and pulmonary vascular resistance and significantly lower cardiac output than the control group. Following the first exercise test only the IPE group were given 50 mg sildenafil orally and after 150 min the measurements during the underwater exercise protocol were repeated. During the repeat exercise after sildenafil, the haemodynamic parameters in the IPE subjects tended to normalise towards the parameters in control subjects without sildenafil, and some parameters were no longer significantly different.

For risk of developing pulmonary oedema, the key measurement is pulmonary capillary pressure. In the controls, pulmonary capillary wedge pressure during exercise was 13.1 ± 5.0 mmHg and in the IPE subjects pre-sildenafil it was 18.9 ± 5.5 mmHg (difference $P = 0.03$). After sildenafil, pulmonary capillary pressure during exercise was 16.9 ± 6.2 mmHg, which was not significantly different from either the control subjects or the IPE subjects pre-sildenafil.

There is no mention of any subject developing IPE during the test, but the haemodynamic comparison of control and IPE subjects before sildenafil suggests that those who had a history of IPE have haemodynamic differences from controls, which are consistent with an increased risk of pulmonary oedema. As such, that comparison of control and IPE subjects was consist with the original report on IPE.[1] The authors acknowledged that performing the post-sildenafil exercise test after the baseline exercise test in the IPE subjects may have influenced the findings after sildenafil. They suggested that sildenafil might be useful in the prevention of IPE.

It has been found previously that nifedipine reduces the pathological vasoconstrictor responses to physiological stimuli in individuals with IPE.[22] Therefore, for more than 30 years, I have advised divers that refused to stop diving after an episode of IPE to take 5 mg nifedipine before diving. I am not aware of recurrence when they did so, but the numbers are small.

The high incidence of IPE in the swimming trials of male military recruits in Israel is supported by data from the Vansbro swimming race (Vansbrosimningen) in Swedish rivers.[23,24] In 2016, 69 of 13,878 (0.5%; 58 of the 69 patients were women) of participants had symptoms varying from coughing to fulminant pulmonary oedema.[23,24] Forty-six patients were treated with CPAP.

A survey in triathletes in the USA reported that 1.4% had experienced symptoms compatible with IPE.[25] In the survey risk factors for IPE were female gender and hypertension. Though IPE appears to be more common in women than in men, research studies have been performed predominantly or exclusively in men.

TAKOTSUBO CARDIOMYOPATHY

There are a small number of case reports of patients who had IPE and Takotsubo cardiomyopathy.[26,27] Takotsubo affects women more frequently than men and particularly affects middle-aged and post-menopausal women, who are the group who get IPE most commonly. Takotsubo cardiomyopathy presents with chest pain more frequently than dyspnoea, whereas the converse is the case with IPE. Many cases of IPE improve within hours of leaving the water, which would not be expected if the aetiology were Takotsubo cardiomyoapthy. Takotsubo cardiomyopathy produces dramatic electrocardiographic and echocardiographic changes, which resolve in days, weeks or months in survivors. These are not found in most people with IPE. Therefore it is possible that when Takotsubo cardiomyopathy and IPE are present in the same patient, the Takotsubo cardiomyopathy is secondary to the stress of having IPE.

Reversible myocardial dysfunction was reported in 15 of 54 consecutive divers with IPE.[14] Myocardial dysfunction was defined as an elevated level of troponin with electrocardiographic and/or echocardiographic abnormalities. The abnormalities in individual patients were described in the table in that paper, but in no case were they consistent with Takotsubo cardiomyopathy. Significantly more of the 15 with myocardial dysfunction were older than 50 years (11 of 15 vs. 13 of 39), hypertensive (nine of 15 vs. six of 39) and diabetic (three of 15 vs. none of 39). Because IPE causes hypoxaemia and because myocardial ischaemia can cause reversible myocardial dysfunction we do not know whether the myocardial dysfunction in these cases contributed to causation of IPE or was the result of IPE.

NEGATIVE PRESSURE BREATHING

There is increasing evidence that divers using closed circuit (CCR) and semi-closed circuit rebreathers are at increased risk of IPE compared to divers using open circuit (see discussion below of divers 10, 11 and 12). The first reported CCR diver was a 20-year-old combat diver using a CCR, who had done 17 previous dives with the equipment, but whether the counter-lung was back- or front-mounted is not stated.[28] The authors noted that "*the pressure difference between the lung centroid and the breathing bag of closed circuit scuba equipment when this is positioned higher than the diver's suprasternal notch, produce transmural pulmonary hydrostatic forces that favor a fluid shift from the pulmonary capillaries to the alveoli*."[28]

A further 11 mine clearance divers who had IPE when using rebreathers have been reported; ten of which were semi-closed circuit rebreathers worn on the back.[29]

The effects of positive and negative pressure breathing at rest and during exercise (i.e., four interventions each for 30 min in random order on separate occasions) were investigated in 16 male professional divers, mean age 34.4 ± 12.1 years.[30] It appears that none had a history of IPE. In the divers orientated prone, breathing with a positive pressure was achieved by attaching a rebreather anteriorly and for negative pressure breathing the rebreather was attached posteriorly. Lung comet score, a grading of extra-vascular lung water detected by ultrasound, was the measure of interstitial pulmonary oedema. The ultrasound comet score was zero following dives at rest regardless of breathing pressure. Following exercise while maintaining the heart rate at 110 bpm, the mean comet score was 4.2 with positive pressure breathing and 15.1 with negative pressure breathing.[30] This study suggests that IPE may occur in fit divers during exertion even if positive pressure breathing but negative pressure breathing increases the risk of IPE.

The same group also described a special forces trainee aged 26 years who had IPE with a front-mounted counter-lung rebreather.[31] The authors demonstrated that when in a head up position in the water with the automatic diluent valve adjusted as the diver had done, he was breathing against a negative pressure.

Swimmers and snorkellers are negative pressure breathers because their lung centroid is below the surface of the water. Their posture in the water will affect the degree of negativity. A scuba diver using a single hose demand valve will be positive pressure breathing if he descends head first and negative pressure breathing during ascent. If using a rebreather, the relative positions of the gas in the counter-lung and the diver's lung centroid will determine the pressure difference. The pressure difference may be dynamic. For example, as a diver in the prone position breathes from a back-mounted counter-lung, the reduction in volume may cause the negative pressure to increase towards end-inspiration for two reasons; 1) all counter-lungs have a degree of elastance and, therefore, the pressure in the counter-lung is slightly greater at the start of inspiration, and 2) during inspiration the volume of gas in the counter-lung will decrease and the distance between the lung centroid and the gas "*level*" in the counter-lung will increase (G Anthony, personal communication, 2018). In addition, resistance to breathing of the equipment may affect generation of negative intrathoracic pressures, particularly as gas density increases with depth.

TIGHT SUIT/EQUIPMENT

Compression from a wetsuit increases urine volume.[32] It is almost certainly the result of an increase in venous return and hence filling pressures. It is possible that a tight wetsuit would also increase pulmonary capillary pressure by the same mechanism.

Illustrative case reports

Therefore, it appears that the risk of experiencing IPE is determined by factors intrinsic to the diver or swimmer and extrinsic factors related to the conditions during immersion and the equipment used during a dive. Investigation and analysis of events may be required to determine causation. Some previously unreported cases have been selected as examples to provide insight into the mechanisms involved. Patients gave consent for publication of the description of their case reports.

Hypertension

Hypertension is the most frequent intrinsic factor found in divers who had IPE. Some were known to have hypertension before they had IPE. Many of those divers stop diving and remain well thereafter. The majority of divers that I see with IPE had it diving in cool UK waters, but as more UK diver travel abroad for diving holidays, a greater number are reporting IPE when immersed in warm waters.

CASE 1

A 67-year-old female had performed 240 dives breathing air on open circuit scuba: 153 in British waters wearing a drysuit and 87 in warm seas wearing a wetsuit. She had dyspnoea, cough and haemoptysis during three warm-water dives (depths 12–30 metres' sea water (msw) at ages 58, 64 and 67. CXR confirmed pulmonary oedema on the last occasion. Apart from hypertension, first found during pregnancy, her cardiac findings, ECG and echocardiogram were normal. A treadmill exercise test was normal except for an exaggerated blood pressure response. She stopped diving and remained well 11 years later.

Some people who get IPE develop hypertension later. Some also had high altitude pulmonary oedema, as occurred in the first case seen in 1977.[9]

CASE 2

A female, who had done 40 dives in warm waters during her vacations, had four episodes of IPE between the ages of 55 and 66 years. Three occurred when scuba diving (depths 14–30 m) breathing air or nitrox 32 on open circuit. One was when snorkelling on the surface. She also had an episode of high altitude pulmonary oedema after a rapid ascent to 14,500 feet in Ecuador. A subsequent ECG, echocardiogram, treadmill exercise test, urinary catecholamine excretion and renal ultrasound were normal. She has not dived for eight years but has continued to snorkel without recurrence of IPE. She subsequently developed hypertension.

Two men had renal artery stenosis (cases 3 and 4). Neither had pulmonary oedema out of the water, but it appears that in these individuals, who had activation of the renin-

angiotensin-aldosterone axis, the additional effects of immersion triggered pulmonary oedema.

CASE 3

A commercial diver had scuba dived since age 14 and done many thousands of uneventful dives. Hypertension was diagnosed at age 48. Between the ages of 49 and 51, he did 65 dives and had nine episodes of severe dyspnoea, sometimes expectorating bloodstained froth. The first episode was when snorkelling in tropical water. Eight episodes were when using open circuit scuba: one was in a heated training pool and six episodes were when diving with air as the breathing gas in tropical water wearing a wet suit. The depths were 6–40 msw. Another diver rescued him because of severe dyspnoea on one occasion.

The eighth episode was when diving to 15 msw in the English Channel, wearing a drysuit and breathing nitrox32. Water temperature was 8°C. He became severely breathless 25 min into the dive. He had bilateral pulmonary crepitations and CXR confirmed pulmonary oedema. Outpatient investigations showed persistent hypertension; left ventricular hypertrophy (LVH) and global impairment of left ventricular (LV) systolic function (ejection fraction 42%) on echocardiography; impaired renal function (glomerular filtration rate 63 $ml \cdot min^{-1}$); normal urinary catecholamine excretion; and a severe stenosis of the left renal artery consistent with fibromuscular dysplasia on a CT angiogram. Following balloon angioplasty of the renal artery stenosis his blood pressure was controlled very well on amlodipine 10 mg daily. He returned to diving and performed hundreds of commercial dives in both tropical and British waters during the next eight years without event.

At age 59 he had another episode of IPE after 30 min when at 16 m depth in 16°C water. (He had performed longer working dives in the two preceding days without problems.) Soon after he surfaced he became unconscious. His initial oxyhaemoglobin saturation in hospital was 79% on 100% oxygen. CXR again confirmed pulmonary oedema. ECG showed lateral T-wave inversion. Measurements of troponin were normal. He improved over two days, but after returning to the UK he had dyspnoea on exertion and nocturnal dyspnoea. Two months later his ECG was unchanged, and an echocardiogram showed LVH with moderate global impairment of LV function. A CT angiogram showed no recurrence of the renal artery stenosis. A myocardial perfusion scan showed no evidence of ischaemia but the LV was dilated with an ejection fraction of 33%. The current diagnosis is LV dysfunction secondary to hypertension. He will not dive again.

In case 4, in addition to renal artery stenosis there were other risk factors for IPE (fluid loading and a long duration dive using a rebreather).

CASE 4

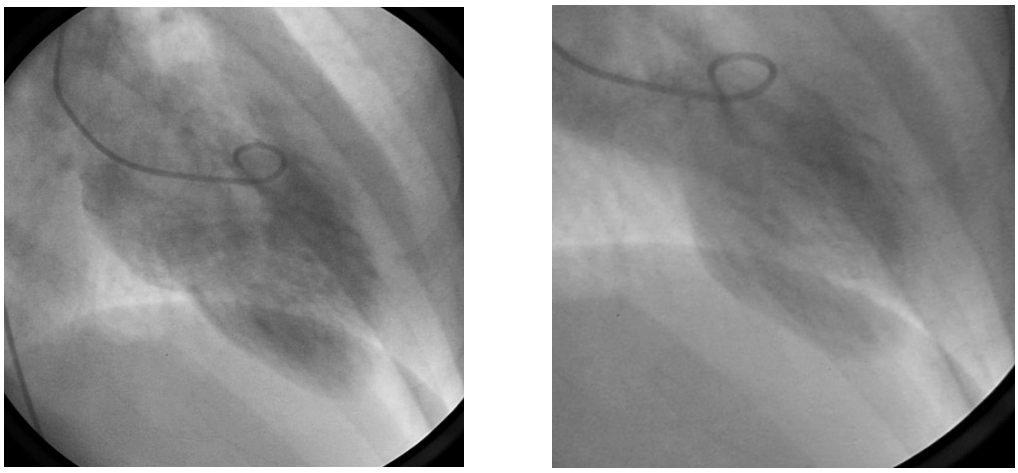
A 57-year-old male with mild hypertension had performed 240 scuba dives in the five years preceding an episode of pulmonary oedema. Most dives were on open circuit scuba, but 72 dives were with a rebreather (Evolution Plus, Ambient Pressure Diving Ltd, Cornwall, UK). For 15 of the dives using the rebreather, the breathing gas was trimix. During a holiday in the tropics, he performed two dives per day for three weeks. The breathing gas on some dives was air on open circuit and on others it was trimix using the CCR. In the few hours before the next deep trimix dive, he drank more than 3 L of fluid. The maximum depth was 89 msw and duration 81 min. He became progressively more breathless from 12 min into the dive with a cough during the ascent, but managed to follow his planned decompression schedule. However, he needed assistance from his dive buddy and about half a metre below the surface he lost consciousness. On regaining consciousness, he expectorated blood-stained froth but had no chest pain. CXR and CT chest showed pulmonary oedema. An ECG showed lateral T-wave inversion. Two weeks later a repeat ECG showed persistence of lateral T-wave inversion, but subsequently the T waves became normal. An echocardiogram showed mild aortic valve thickening without stenosis and good LV function. During a treadmill exercise test, he completed 12 min of the Bruce protocol without chest pain or ECG changes. Blood pressure rose to 190/100 on exercise. An MRI angiogram showed stenosis of the left renal artery. The kidneys and the adrenal glands were normal. The stenosed left renal artery was stented. Since returning to diving, he has performed 160 dives - using a CCR for 121 dives (deepest 101 msw and longest over 185 min) and using open circuit for 39 dives. without recurrence of symptoms. He now avoids over-hydration before dives.

Case 5 also suggested the possibility of excessive activity of the renin-angiotensin-aldosterone axis as a contributor to IPE in some cases.

CASE 5

A 47-year-old female had done 357 uneventful dives before having pulmonary oedema when diving to 30 msw, breathing air on open circuit scuba in British waters. It was the first day of her menstrual cycle. Her weight often increased 1.5 kg at the start of menstruation. Before this particular dive, she had peripheral oedema and felt bloated, which was not unusual at that stage of her cycle. She had cough and dyspnoea 21 min into the dive. Her consciousness level was impaired. CXR confirmed pulmonary oedema. Oxyhaemoglobin saturation was 84%. Cardiac enzymes and ECGs were normal. An echocardiogram four days later was normal. Lung function tests and treadmill exercise tests were normal. In the subsequent 10 years she has been well, with normal blood pressure and she has done about 50 uneventful shallow dives.

Figure 2
Left ventriculogram of Case 7 who had Takotsubo cardiomyopathy associated with immersion pulmonary oedema, showing the end diastolic frame (left panel) and end systolic frame



Case 5 had pulmonary oedema on the first day of menstruation when she was oedematous. Fluid retention in the late-luteal phase of the menstrual cycle is related to activation of the renin-angiotensin-aldosterone axis.[33] Pulmonary oedema at the time of menstruation in 14 consecutive menstrual cycles was reported in a woman with mitral stenosis and was attributed to fluid retention and increased blood volume.[34]

Other cardiac diseases

As stated before, hypertension is the most common cardiovascular finding in divers presenting with IPE. Most have preserved LV function, but some have LV systolic dysfunction on an echocardiogram and/or a cardiac MRI scan, but without significant coronary narrowing or evidence of myocardial infarction. In a far smaller number of cases, IPE is the presenting event in divers who have significant coronary artery disease, dilated cardiomyopathy or valvular disease.

CASE 6

A 56-year-old male had two episodes of pulmonary oedema during consecutive shallow dives using open circuit scuba in tropical water. His work involved heavy lifting but he had no cardiac symptoms in everyday life. He had dived for 10 years but only on his annual vacations in tropical water. He became unusually breathless during his first dive of a holiday, a gentle dive to 8 msw for 55 min, but he recovered quickly afterwards. The next day, 13 min into another 8 msw dive he had cough and severe dyspnoea. He had signs and the CXR appearances of pulmonary oedema. There was a loud mitral systolic murmur. Cardiac enzymes and an ECG were normal. An echocardiogram showed that the left ventricle was mildly dilated with prolapse of the posterior mitral valve leaflet causing moderate mitral regurgitation into a dilated left atrium. Cardiac catheterisation showed pulmonary artery pressure 62/24, mean 40 mmHg; mean pulmonary capillary wedge pressure 23 mmHg; left ventricular end diastolic pressure 29 mmHg; and aortic pressure 117/73 mmHg. Coronary angiography showed severe stenoses in the proximal left anterior descending and right coronary arteries. He had a mitral valve repair and two coronary artery bypass grafts. He has not dived again in eight years following surgery.

Takotsubo cardiomyopathy and emotional stress

Takotsubo cardiomyopathy has been described in association with IPE.[26,27] I have seen only one case.

CASE 7

A 59-year-old female had done over 600 dives in 27 years and developed pulmonary oedema during a dive to 29 msw for 33 min off the Canary Islands. She breathed air on open circuit scuba. She wore a wetsuit, but felt cold. She had dyspnoea without chest pain and expectorated bloodstained froth. CXR confirmed pulmonary oedema. Blood gases showed severe hypoxaemia. Her ECG showed ST elevation evolving to T-wave inversion in anterior and inferior leads and Troponin T was elevated. Two days later, a coronary arteriogram showed normal coronary arteries. The left ventriculogram was typical of Takotsubo cardiomyopathy (Figure 2). Four months later blood pressure was 180/80, but ECG, CXR and echocardiogram were normal. During a treadmill exercise test she completed 11 minutes of the Bruce protocol without abnormality. She did not dive in the subsequent four years and remained well, but has hypertension.

In this and other cases there is uncertainty whether the Takotsubo cardiomyopathy was the cause of IPE or the result of the stress of the events. Certainly, other divers

with stressful episodes precipitating IPE have no evidence of Takotsubo cardiomyopathy (Cases 8 and 9).

CASE 8

A 65-year-old male had performed over 1,000 dives before he had an episode of immersion pulmonary oedema during a highly stressful dive to 30 msw using open circuit scuba in the Mediterranean. Clinical features of IPE were confirmed by CXR and CT chest; ECG and troponin were normal. During a treadmill exercise test there was an exaggerated blood pressure response (maximun 230/95). Ambulatory blood pressure recording confirmed hypertension. An echocardiogram showed concentric LVH, confirmed on a cardiac MRI scan, but there was no evidence of ischaemia, infarction or fibrosis. Urinary catecholamine and cortisol excretion, plasma aldosterone and renin concentrations and a renal ultrasound were normal. In the six years since his episode of IPE he has continued diving without recurrence.

CASE 9

A 53-year-old female had performed more than 1,000 uneventful dives using open circuit scuba in 29 years. Most were in the UK. She then performed two uneventful dives one day in Scottish waters wearing a neoprene drysuit. The next day she felt congested and took a proprietary brand of pseudoephedrine 60 mg one hour before a 47 msw dive breathing air. She had not used pseudoephedrine for 10–15 years. It was dark and she became separated from her buddy. She felt stressed. During the ascent she started to cough, had chest tightness and felt breathless. On the surface she coughed up bloodstained froth. Oxyhaemoglobin saturation was 80%. CXR showed widespread pulmonary oedema. An ECG was normal apart from sinus tachycardia. Cardiac enzymes were normal. She was treated with CPAP. Blood pressure, an echocardiogram, a cardiac MRI and stress perfusion imaging were normal. She has not dived in three years since she had IPE and remains well.

This experienced diver had IPE after a stressful dive and after she had taken pseudoephedrine. Takotsubo-like myocardial dysfunction can be associated with phaeochromocytoma.[35] Pseudoephedrine has sympathomimetic properties, but she had no evidence of Takotsubo cardiomyopathy. She was not and is not hypertensive, but pseudephedrine causes vasoconstriction and can increase blood pressure.[36] It is possible that in a situation when there was increased preload from immersion and increased afterload from cold exposure, the combination of stress and pseudoephedrine acted synergistically to precipitate IPE.

IPE during use of a rebreather

A number of divers who had dived for years without problems had episodes of IPE soon after starting to use a rebreather, particularly when there was a back-mounted counter-lung. Case 10 is an example.

CASE 10

A 29-year-old male had a single episode of pulmonary oedema during his thirteenth dive using a CCR (Inspiration Vision, Ambient Pressure Diving Ltd, Cornwall, UK) and breathing nitrox. He had performed about 300 dives in cool British waters and about 100 dives in warmer seas using open circuit scuba without problems. He breathed air on about half the dives and nitrox on the others. The deepest dive was 44 msw. He did four uneventful training dives with the CCR before he went on a trip to the Orkney Isles. The episode of pulmonary oedema occurred on the ninth dive of the trip. The maximum depth of the dive was 38 msw. Cough and dyspnoea started about 30 min into the dive when at 25 msw. He expectorated bloodstained froth. He had bilateral pulmonary crepitations. Oxyhaemoglobin saturation was 94%. CXR confirmed pulmonary oedema. Subsequently his blood pressure, cardiovascular examination, an ECG, echocardiogram, treadmill exercise test, urinary catecholamine excretion and CT renal angiogram were all normal. He has stopped diving and has been well without cardiac problems in the subsequent seven years.

CASE 11

A scuba instructor was first seen at age 43 years. He is now age 50. Over 24 years he had performed more than 2,000 uneventful dives using open circuit scuba with breathing gases being air, nitrox and trimix (deepest 96 msw). He also used rebreathers for about 150–200 dives, breathing nitrox and trimix. The average duration of dives using the rebreather was approximately 90 min. When first seen he described five episodes of dyspnoea, wheeze, cough and expectorated bloodstained froth when diving using a CCR with a back mounted counter-lung (Ouroboros, VR Technology Ltd, Dorset, UK).

CXR confirmed pulmonary oedema on one occasion. All five episodes of pulmonary oedema occurred when he used the CCR in cool British waters. He did not have episodes when using the rebreather in warm water or when using open circuit in cold or warm water. Some IPE episodes occurred when breathing nitrox and others occurred when breathing trimix with depths of dives from 30–84 msw. The onset of episodes was consistently 25–30 min into the dive, but he had no symptoms on some longer dives (over 90 min duration). Blood pressure, cardiovascular findings, ECG and echocardiogram were normal. During a treadmill exercise test he completed 19 min of the Bruce protocol without difficulty. He also described occasional irregular palpitations.

He returned to diving predominantly using open circuit scuba but occasionally using the Ouroboros CCR. At age 45, he reported another episode of IPE when diving in cold water using his CCR. Then at age 46, he had pulmonary oedema using the Ouroboros in warm water in Florida when he had to swim hard against a current. At age 48 he had IPE with

expectoration of blood-stained froth when he snorkelled rapidly in a wet suit across a cold lake in the UK. He tried diving using other rebreathers, including five dives on the Sentinel CCR (VR Technology Ltd, Dorset, UK). At age 49 he performed two dives in one day in a lake in the UK wearing a dry suit and using the Sentinel. The first was for 32 min duration. He started to wheeze 58 min into the second dive and on surfacing expectorated pink froth. Subsequently he developed persistent atrial fibrillation requiring catheter ablation. His blood pressure remains normal.

Case 11 initially had IPE only when using a CCR in cold water, but later had IPE when using it on a dive in warm water when there was significant exertion and when snorkelling rapidly in cold water. Later he had IPE when using a different make of rebreather that also has a back mounted counter-lung. Subsequent onset of atrial fibrillation raises the possibility of LV diastolic dysfunction in the absence of hypertension. It appears that Case 11 had IPE only when there were at least two of three risk factors that increased the pressure gradient across the pulmonary capillaries, namely negative pressure breathing from a rebreather with a back mounted counter-lung, cold and/or exertion.

In some cases the onset of symptoms appears linked to an event during use of a rebreather that increased negative inspiratory pressure.

CASE 12

A 48-year-old male had performed more than 100 dives on open circuit with durations up to 80 min and a number of triathlons without problems. He performed eight training dives with a CCR with a back mounted counter-lung (RedBare, Vobster Marine Systems, Somerset, UK). His next dive was his first recreational dive with this CCR. He drank a litre of fluids in the four hours before the dive. Water temperature was 5°C. He wore a drysuit. After 40 min at 10 m he descended to practice manual injection of diluent but failed to inject the diluent quickly enough and tried to inhale from an under-filled counter-lung, exerting a forceful negative pressure as he did so. He immediately experienced difficulty breathing. After surfacing he expectorated blood streaked frothy sputum. He was found to have hypertension, but an ECG, an echocardiogram, CT coronary angiogram and renal function were normal.

In Case 12, a single inspiration with forceful negative pressure appears to have triggered the onset of IPE. This is analogous to attempted inspiration with laryngeal obstruction.

Medical conditions

Some medical conditions may also increase negative pressures during inspiration.

CASE 13

A 45-year-old female had four episodes of IPE in 26 dives using open circuit scuba. The first was on her third dive and was in the UK. She became breathless after 6 min at 7 msw. After surfacing she coughed up frothy sputum. Next, she was breathless after a surface swim to a dive site in Fiji and had to abort the dive almost immediately she started to descend. The last two episodes occurred on consecutive days in the Mediterranean. On each occasion she became breathless soon after the start of the dive and on surfacing coughed up bloodstained froth. Symptoms resolved in between one and three hours. Blood pressure, ECG and echocardiogram were normal. She has Ehlers Danlos syndrome with a history of joint dislocation and an abnormally mobile trachea such that she finds that she needs to sleep with her neck in a certain position to prevent her waking with choking at night. She uses CPAP for sleep apnoea. Lung function tests and a CT chest were normal. She has stopped diving.

The lack of rigidity of the airway in Ehlers Danlos syndrome can cause dynamic extrathoracic airway obstruction.[37–39] Dynamic extrathoracic airway obstruction causes the greatest limitation of flow during inspiration, when subatmospheric intraluminal pressure draws the obstructing lesion inward, reducing the diameter of the airway lumen.[40] It can cause pulmonary oedema unconnected with immersion.[41] It is possible that in case 13, dynamic extrathoracic airway obstruction from her Ehlers Danlos syndrome coupled with the transpulmonary pressure gradient during immersion acted in synergy to increase negative airway pressures during inspiration, which coupled with other effects of immersion, caused IPE.

Death from IPE

IPE can cause sufficient hypoxia to result in unconsciousness, so it is probable that it can cause death. Some deaths from IPE have been described in the literature.[8,42,43] In the UK, coroners have certified IPE as the cause of some diving deaths.

Making a diagnosis of IPE in a diver or swimmer who survives and is able to give a history of the events is much easier than making a diagnosis of IPE in someone who has died. At post mortem examination it may be difficult to distinguish pulmonary oedema fluid from inhaled fluid. The greater difficulty is that pulmonary oedema formation after death is very common and particularly so when resuscitation is attempted.[44] The reason is that when cardiac function ceases in a normally hydrated person, all intravascular pressures equalise at approximately 40 mmHg – not at zero. A pulmonary capillary pressure of 40 mmHg exceeds the plasma oncotic pressure and transudation occurs. During efficient cardiac massage forward flow occurs so more blood enters the pulmonary capillaries from the right heart to replace the plasma that has passed into the alveoli. In

addition, during chest compression, all cardiac chambers are compressed, so there is backpressure from the left atrium to pulmonary capillaries. Therefore, unless a person dies from haemorrhage or is severely hypovolaemic at the time of death, pulmonary oedema is the usual pulmonary finding at post mortem.[44]

Therefore, in order to diagnose IPE as the cause of death one needs to rely on other indirect evidence. It might be that other divers observe that the diver was breathing rapidly for no obvious reason or see a change to a secondary breathing gas supply when the primary gas supply is later found to be working satisfactorily. Occasionally there is photographic or video evidence of the events to suggest IPE.

Using such evidence, it seems probable that IPE is the cause of death in a significant number of UK divers who died. In particular, some very experienced UK scuba divers, who had performed thousands of dives over many years, appear to have died from IPE during their earliest dives, often training dives, using rebreathers.

References

1 Wilmshurst PT, Nuri M, Crowther A, Webb-Peploe MM. Cold-induced pulmonary oedema in scuba divers and swimmers and subsequent development of hypertension. Lancet. 1989;I:62–5. doi:10.1016/S0140-6736(89)91426-8. PMID:2562880.

2 Ganong WF. Review of medical physiology. Los Altos, California; Lange Medical Publications: 1969. p. 16.

3 Rassler B. Contribution of α and β–adrenergic mechanisms to the development of pulmonary oedema. Scientifica. 2012:829504. doi:10.6064/2012/829504. PMID: 24278744. PMCID: PMC3820440.

4 Guinard JP. Laryngospasm-induced pulmonary oedema. Int J Pediatr Otorhinolaryngol. 1990;20:163–8. PMID:2286509.

5 Moore RL, Binger CA. The response to respiratory resistance: a comparison of the effects produced by partial obstruction in the inspiratory and expiratory phases of respiration. J Exper Med. 1927;45:1065–80. PMID: 19869306. PMCID: PMC2131159.

6 Engoren MC. Negative-pressure pulmonary oedema with a patent airway. J Burn Care Rehabil. 1998;19:317–20. PMID: 9710729.

7 Nolan J, Greenwood J, Mackintosh A. Cardiac emergencies: a pocket guide. Oxford; Butterworth Heinemann: 1998. p. 69–73.

8 Wilmshurst P. Heart failure when diving. Proceedings of the diving officers' conference. Location; British Sub-Aqua Club: 1984. p. 39–42.

9 Wilmshurst PT. Pulmonary oedema induced by emotional stress, by sexual intercourse, and by exertion in a cold environment in people without evidence of heart disease. Heart. 2004;90:806–7. doi:10.1136/hrt2002.005595. PMID: 15201259. PMCID: PMC1768332.

10 Wilmshurst P, Nuri M, Crowther A, Betts J, Webb-Peploe MM. Forearm vascular responses in subjects who developed recurrent pulmonary oedema when scuba diving: a new syndrome. Br Heart J. 1981;45:349.

11 Wilmshurst PT, Nuri M, Crowther A, Betts JC, Webb-Peploe MM. Recurrent pulmonary edema in scuba divers: prodrome of hypertension: a new syndrome. Underwater Physiology VIII. In: Bachrach JJ, Matzen MM, editors. Bethesda, Maryland; Undersea Medical Society Inc: 1984. p. 327–39.

12 Arborelius M, Balldin UI, Lilja B, Lundgren CEG. Hemodynamic changes in man during immersion with the head above water. Aerosp Med. 1972;43:592–8. PMID: 5035546.

13 Wood DL, Sheps SG, Elveback LR, Schirger A. Cold pressor test as a predictor of hypertension. Hypertension. 1984;6:301–6. PMID: 6735451.

14 Gempp E, Louge P, Henckes A, Demaistre S, Heno P, Blatteau J-E. Reversible myocardial dysfunction and clinical outcome in scuba divers with immersion pulmonary oedema. Am J Cardiol. 2013;111:1655–9. doi:10.1016/j.amjcard2013.01.339. PMID: 2349776.

15 Gempp E, Demaistre S, Louge P. Hypertension is predictive of recurrent immersion pulmonary edema in scuba divers. Int J Cardiol. 2014;172:528–9. doi:10.1016/j.ijcard2014.01.021. PMID: 24485632.

16 Pons M, Blickenstorfer D, Oechslin E, Hold G, Greminger P, Franzeck UK, et al. Pulmonary oedema in healthy persons during scuba-diving and swimming. Eur Respir J. 1995;8:762–7. PMID: 7656948.

17 Weiler-Ravell D, Shupak A, Goldenberg I, Halpern P, Shoshani O, Hirschhorn G et al. Pulmonary oedema and haemoptysis induced by strenuous swimming. BMJ. 1995;311:361–2. PMID: 7640542. PMCID: PMC2550430.

18 Adir Y, Shupak A, Gil A, Peled N, Keynan Y, Domachevsky L, et al. Swimming-induced pulmonary edema: clinical presentation and serial lung function. Chest. 2004;126:394–9. doi:10.1378/chest.126.2.394. PMID: 15302723.

19 Slade JB, Hattori T, Ray CS, Bove AA, Cianci P. Pulmonary edema associated with scuba diving. Chest. 2001;120:1686–94. PMID: 11713154.

20 Peacher DF, Martina SD, Otteni CE, Wester TE, Potter JF, Moon RE. Immersion pulmonary edema and comorbidities: case series and updated review. Med Sci Sports Exerc. 2015;47:1128–34. doi: 10,1249/MSS.0000000000000524. PMID: 25222821.

21 Moon RE, Martina SD, Peacher DF, Potter JF, Wester TE, Cherry AD, et al. Swimming-induced pulmonary edema: pathophysiology and risk reduction with sildenafil. Circulation. 2016:133:988–96. doi: 10.1161/CIRCULATIONAHA.115.019464. PMID: 26882910. PMCID: PMC5127690.

22 Wilmshurst P. Cardiovascular problems in divers. Heart. 1998;80:537–8. PMID:10065018. PMCID: PMC1728859.

23 Eriksson AB, Annsberg M, Hardstedt M. Simningsorsakat lungodem vid svenska forhallanden otillrackligt studerat: erfarenheter fran Vansbrosimningen. 2016. [cited 2018 December 02]. Available from: http://sanma.se/resources/SIPE_LT_2017_114.pdf. Swedish with English abstract. PMID: 28632299.

24 Eriksson AB, Hardstedt M. The "*Vansbrosimningen*" experience – incidence of swimming induced pulmonary edema (SIPE) and organization of prehospital medical resources. Scienta et Valebrat IV: 2017. p. 9&11. [cited 2018 December 02]. Available from: http://sanma.se/resources/Scientia-et-Valebat-IV-2017.pdf.

25 Miller CC, Calder-Becker K, Modave F. Swimming-induced pulmonary edema in triathletes. Am J Emerg Med. 2010;28:941–6. doi: 10.1016/j.ajem.2009.08.004. PMID: 20887912.

26 Chenaitia H, Coullange M, Benhamou L, Gerbaux P. Takotsubo cardiomyopathy associated with diving. Eur J Emerg Med.

2010;17:103–6. doi: 10.1097/MEJ.06013e32832dd8ee. PMID: 19543098.
27 Ng A, Edmonds C. Immersion pulmonary oedema and Takotsubo cardiomyopathy. Diving Hyperb Med. 2015;45:255–7. PMID: 26687314.
28 Shupak A, Guralnik L, Keynan Y, Yahir Y, Adir Y. Pulmonary oedema following closed-circuit oxygen diving and strenuous swimming. Aviat Space Environ Med. 2003;74:1201–4. PMID: 14620479.
29 Gempp E, Louge P, Blatteau JE, Hugon M. Descriptive epidemiology of 153 diving injuries with rebreathers among French military divers from 1979 to 2009. Mil Med. 2011;176:446–50. PMID: 21539168.
30 Castagna O, Regnard J, Gempp E, Louge P, Brocq FX, Schmid B, et al. The key role of negative pressure breathing and exercise in the development of interstitial pulmonary edema in professional male scuba divers. Sports Med-Open. 2018;4:1. doi: 10.1186/s40798-017-0116-x. PMID: 29299780. PMCID: PMC5752643.
31 Castagna O, de Maistre S, Schmid B, Caudal D, Regnard J. Immersion pulmonary oedema in a healthy diver not exposed to cold or strenuous exercise. Diving Hyperb Med. 2018;48:40–4. doi: 10.28920/dhm48.1.40-44. PMID: 29557101.
32 Castagna O, Blatteau J-E, Vallee N, Schmid B, Regnard J. The underestimated compression effect of neoprene wetsuit on divers hydromineral homeostasis. Int J Sports Med. 2013;34:1043–50. doi:10.1055/s-0033-1345136. PMID: 23780899.
33 Sundsfjord JA, Aakvaag A. Plasma angiotensin II and aldosterone excretion during the menstrual cycle. Acta Endocrinol. 1970;64:452–8. PMID: 4318141.
34 Edeiken J, Griffith JQ. Cyclic pulmonary edema at menses in mitral stenosis. Relief following irradiation of pituitary gland. JAMA. 1940;115:287–9.
35 Ghadri J-R, Wittstein IS, Prasad A, Sharkey S, Dote K. Akashi YJ, et al. International Expert Consensus Document on Takotsubo Syndrome (Part 1): clinical characteristics, diagnostic criteria, and pathophysiology. Euro Heart J. 2018;39:2032–46. doi: 10.1093/eurheartj/ehj076. PMID: 29850871. PMCID: PMC5991216.
36 Cantu C, Arauz A, Murillo-Bonilla LM, Lopez M, Barinagarrementeria F. Stroke associated with sympathomimetic contained in over-the-counter cough and cold drugs. Stroke. 2003;34:1667–73. doi: 10.1161/01.STR.0000075293.45936.FA. PMID: 12791938.
37 Seebald J, Muscarella J. Ehlers-Danlos presenting as airway obstruction and hoarseness. J Case Med Rep. 2015;4:235956. doi: 10.4303/jcrm/235956.
38 Chatzoudis D, Kelly TJ, Lancaster J, Jones TM. Upper airway obstruction in a patient with Ehlers-Danlos Syndrome. Ann R Coll Surg Engl. 2015;97:e50–1. doi: 10.1308/003588414X14055925061793. PMID: 26263828. PMCID: PMC4474037.
39 Safi FA, Alyosif MA, Imam S, Assaly RA. Arytenoid prolapse in 3 patients with Ehlers-Danlos Syndrome leading to respiratory compromise. Mayo Clin Proc. 2017;92:851–3. doi: 10.1016/j.mayocp2017.06.016. PMID: 28473043.
40 Pradhan D, Berger K. Dynamic extrathoracic airway obstruction. N Engl J Med 2012;367:e2. doi: 10.1056/NEJMicm1010669. PMID: 22762344.
41 Lang SA, Duncan PG, Shepherd DA, Ha HC. Pulmonary oedema associated with airways obstruction. Can J Anaesth. 1990;37:210–8. doi: 10.1007/BF03005472. PMID: 2178789.
42 Edmonds C, Lippman J, Lockley S, Wolfers D. Scuba divers pulmonary oedema: recurrence and fatalities. Diving Hyperb Med. 2012;42:40–4. PMID: 22437975.
43 Smart D, Sage M, Davis FM. Two fatal cases of immersion pulmonary oedema – using dive accident investigation to assist the forensic pathologist. Diving Hyperb Med. 2014:44:97–100. PMID: 24986728.
44 Durlacher SH, Banfield WG Jr, Bergner AD. Post-mortem pulmonary edema. Yale J Biol Med. 1950;22:565–72. PMID: 15431685. PMCID: PMC2599206.

Conflicts of interest and funding: nil

Submitted: 20 August 2018; revised 14 January 2019
Accepted: 14 January 2019