TRANSCRANIAL DOPPLER ULTRASOUND AND THE
ETIOLOGY OF NEUROLOGIC DECOMPRESSION SICKNESS
DURING ALTITUDE DECOMPRESSION

W. T. Norfleet, M. R. Powell, K. V. Kumar*, and J. Waligora
Space Biomedical Research Institute and *KRUG Life Sciences
NASA/Johnson Space Center, Houston, Texas 77058

ABSTRACT The presence of gas bubbles in the arterial circulation can occur from iatrogenic mishaps, cardiopulmonary bypass devices, or following decompression, e.g., in deep-sea or SCUBA diving or in astronauts during extravehicular activities (EVA). We have examined the pathophysiology of neurological decompression sickness in human subjects who developed a large number of small gas bubbles in the right side of the heart as a result of hypobaric exposures. In one case, gas bubbles were detected in the middle cerebral artery (MCA) and the subject developed neurological symptoms; a "resting" patent foramen ovale (PFO) was found upon saline contrast echocardiography. A PFO was also detected in another individual who developed Spencer Grade IV precordial Doppler ultrasound bubbles, but no evidence was seen of arterIALIZATION of bubbles upon insonation of either the MCA or common carotid artery. The reason for this difference in the behavior of intracardiac bubbles in these two individuals is not known. To date, we have not found evidence of right-to-left shunting of bubbles through pulmonary vasculature. The volume of gas bubbles present following decompression is examined and compared with the number arising from saline contrast injection. The estimates are comparable.

INTRODUCTION
A. DECOMPRESSION SICKNESS

1. Manifestations

Decompression sickness (DCS) can manifest itself in many forms dependent upon (i) the site of gas phase growth in the tissues or (ii) migration of bubbles by the blood stream. The forms generally include the following although this listing is not complete (missing, for example, is lymphatic obstruction):

(a) neurologic DCS from the formation of gas bubbles in the brain or spinal cord, or from gas embolization of the brain or cord,

(b) joint-pain DCS from the formation of a gas phase in the connective tissues (tendons, ligaments) of joints,

(c) "the chokes" from the accumulation of gas bubbles in the pulmonary vasculature,

(d) "skin bends" and pruritis from the formation of gas bubbles (purportedly) in the capillaries of the skin,

(e) the "staggers" from the formation of a gas phase in the cerebellum or VIIIth cranial nerve or the organs of balance,

(f) cardiovascular collapse from the appearance of a very large gas bubble load in the right heart leading to a great reduction in cardiac output,

(g) dysbaric osteonecrosis, presumably from the presence of a gas phase in bone.

2. NASA Interest in Cerebral Gas Bubbles

The present study was conducted to
investigate the development and pathophysiology of intravascular gas bubbles arising from decompressions to hypobaric conditions, a process that is a part of extravehicular activities. As a portion of this work, provisions were made for (i) the detection of decompression gas bubbles in the arterial circulation of human subjects, and (ii) screening for the presence of patent atrial septal defects (ASDs) by means of B-mode ultrasound and saline contrast echocardiography. Individuals with a patency were not excluded since:

(1) Current evidence is indecisive with regard to the relationship between an ASD and an increased incidence of neurologic DCS in SCUBA divers. Wilmshurst et al. (1990) found a prevalence of patent right-to-left shunts of 25% (26/105) in a subgroup never experiencing DCS versus a prevalence of 24% (8/34) in a group experiencing late neurologic DCS and 15% (3/20) for joint-pain DCS.

(2) No studies indicate that subjects with numerous decompression gas bubbles (e.g., Spencer Grade IV) develop central nervous system (CNS) DCS or peripheral nerve involvement with an incidence of approximately 25%. This might be expected since the prevalence of PFOs in a population determined post-mortem is ~ 20 to 30%.

(3) The presence of a PFO is not medically disqualifying for astronauts, i.e., candidates are not currently eliminated from astronaut selection because of such a right-to-left shunt.

Clinically, the detection of a PFO involves echocardiographic imagery during intravenous injections of microbubbles in saline followed by a respiratory maneuver intended to provoke shunting of bubbles across the atrial septum. If bubbles are not detected in the left ventricle by means of a transthoracic imaging device, many practitioners elect to utilize a trans-esophageal imager, a noxious test for the patient. Other methods that have been suggested for detecting "arterialization" of gas bubbles include monitoring of the ascending aorta and the middle cerebral artery (MCA) utilizing a range-gated Doppler device.

In the present study during both saline contrast injections and hypobaric decompressions, the following were assessed:

(i) detection of gas bubbles in the pulmonary arteries, and/or
(ii) detection of gas bubbles in the MCA or the ascending aorta.

B. BACKGROUND HYPOTHESIS: CEREBRAL GAS BUBBLES

Inert gas bubbles possessing a radius of less than 50 microns have their genesis in tissue capillaries during decompression and then are released during muscle contraction into the central venous return. As a consequence of their small diameter, they may not be completely sequestered by the pulmonary vascular filter. Questions concerning these gas bubbles are:

(i) If present, could they represent a potential source of emboli and act as causative agents of subtle neurologic lesions in astronauts during EVA?

(ii) If present, can these inert gas microemboli be detected easily and non-invasively in the middle cerebral artery (MCA) of human subjects by utilizing transcranial Doppler ultrasonography?

C. PULMONARY GAS EMBOLISM AND ARTERIALIZATION

Embolization of the central nervous system by inert gas bubbles arising within or entering into the systemic arteries is at least a theoretical possibility whenever a large change of ambient pressure occurs and an inert gas is being breathed. These gas bubbles may result from:

(i) de novo genesis in the arteries
(Brubakk et al., 1981),
(ii) release from supersaturated
tissues into the venous return with subsequent transpulmonary transport (Emerson et al., 1967; Powell, 1977), (iii) rupture of small airways (Walt et al., 1967).

Numerous studies have investigated the question of pulmonary gas embolism over the years. However, these investigations have treated the situation where the gas bubbles existent in the vena cava have been large (approximately 0.1 to 1 mm in radius) (Durant et al., 1947; Spencer and Oyama, 1971; Powell and Johanson, 1978; Powell et al., 1982). Mechanisms for passage to the arterial system have been recognized for many years; they include normal and well-defined anatomical shunts such as pulmonary arteriovenous anastomoses, bronchial venous shunts, large pleural capillaries (Catchpole and Gersch, 1947; Haymaker and Johnson, 1955; Wittmer, 1962), and pathologies such as patent foramen ovale.

Hills and Butler (1981) have stated that the surface tension of gas bubbles actually encountered in body tissues should be less than the theoretical value of 50 dynes/cm². This large value for surface tension yields a retarding pressure of 150 torr for a bubble of 5 micra. A reduction of surface tension to 2 dyne/cm² can be produced by dipalmitoyl lecithin (DPL), a normal lung surfactant. DPL can also induce a contact angle of up to 70°, thus reducing the retarding pressure to approximately 3 torr.

Powell and Spencer (1980) reported that when gas was introduced into the venous return of sheep not by means of a catheter that would generate large gas bubbles (> 0.1 mm radius) but rather by means of small gas bubbles spawned in tissues following decompression (with the creation of microbubbles), the results were opposite. In this latter case, "arterialization", or the passage of gas bubbles from the venous circulation into the systemic arterial circulation, was not uncommon even in the absence of an elevation of the right ventricular systolic pressure (RVSP).

D. CENTRAL NERVOUS SYSTEM (CNS) DECOMPRESSION SICKNESS

In general, the involvement of the central nervous system (CNS) in decompression sickness has been considered to be uncommon. However, some studies have indicated a greater degree of involvement. A number of investigations (Kelly and Peters, 1975; Levin, 1975; Peters et al., 1977) demonstrated that neurological and psychological problems exist following CNS decompression sickness. The problems noted, in order of frequency, were: personality change, headache, recent memory impairment, disco-ordination, paresthesia and weakness, hearing loss, vertigo, urinary symptoms, and dysphasia. Impaired divers also demonstrated low scores on verbal and non-verbal portions of the Wechsler Adult Intelligence Scale; the manner in which the subjects were divided (test and control) makes these studies less than ideal, however.

Deep sea divers with decompression sickness have a high incidence of subtle, subjective complaints such as lethargy, confusion and mental cloudiness, and a general perception that all is not well; this may indicate cerebral involvement. Many of these symptoms have also been experienced by individuals who have undergone a safe decompression, and who have not experienced what classically would be called frank decompression sickness.

E. NEUROLOGIC SEQUELAE

The presence of detectable gas bubbles in the middle cerebral artery (MCA) is not prima facie evidence that neurologic damage is occurring. Possible untoward events could be mitigated by several factors:

(i) The presence of numerous overlapping collaterals would serve to protect brain tissue from anoxia if embolism is not extensive.
(ii) The gas bubbles are composed primarily of oxygen and would dissolve and be metabolically consumed by the tissues of the brain even if they were able to embolize the capillaries. Arterial gas emboli that appeared in the early portion of the decompression, when the brain is not yet denitrogenated, would be considered to be the most pathogenic from a neurologic perspective.

(iii) Numerous air bubbles have been detected by means of surgically implanted Doppler ultrasound probes placed around the carotid artery of sheep (Powell and Spencer, 1981); these subjects rarely demonstrated evidence of neurologic damage.

(iv) Spencer (1990) and Powell (unpublished observations) have noted both gaseous and formed element emboli in the MCA while monitoring with the transcranial Doppler (TCD) at surgery. Spencer reports that a post-operative analysis of 100 TCD monitorings demonstrated gaseous emboli in 44 patients and formed element emboli in 11 patients. Only one patient gave evidence of post-operative stroke; the bubble emboli were detected for 14 seconds in this individual. Two patients with extensive formed-element emboli sustained severe post-operative strokes.

(v) Last, we might consider historical evidence. Human subjects have utilized many decompression profiles in the past with no obvious evidence of CNS involvement. If gas bubbles are detected in the MCA, however, it would be prudent to consider the initiation of a program of psychometric testing as has been done with deep sea divers (Vaernes et al., 1989).

F. TRANSCRANIAL DOPPLER (TCD) ULTRASONOGRAPHY

Aaslid et al. (1982) discovered that the vessels of the brain could be interrogated non-invasively by means of Doppler ultrasound. Placement of a hand-held probe over the temporal region of the skull will position it over a relatively thin region of osseous tissue. With proper angulation, the ultrasound beam can be made to insonate the major blood vessels of the brain including the deep-lying circle of Willis.

The blood vessel which is the easiest to locate and most utilized for intracranial hemodynamic monitoring is the middle cerebral artery (MCA). Gas bubbles present in the MCA produce very intense reflections of the transmitted ultrasound signal superimposed upon the normal blood flow signal. Bubbles that may have escaped the pulmonary filter could be detected with ease as either discrete reflections (Aaslid and Lindgaard, 1986; Spencer 1990) or from the increase in the Doppler signal intensity (Ries et al., 1989).

G. DETECTION OF GAS BUBBLES IN THE CEREBRAL CIRCULATION

Gas bubbles of a radius equal to or greater than 50 microns are expected to give discrete reflections. Gas bubbles smaller than this could be expected to reveal their presence by a modification of the pattern of blood flow.

The amplitude of the reflected Doppler ultrasound beam is a function of the difference in acoustic impedance between the conducting medium (serum) and the individual scattering sites. This difference is modest for erythrocytes but is compensated by their large numbers. The difference between the acoustic impedance of gas bubbles and serum is very high; this will produce an increase in the returned signal intensity even when discrete, individual bubbles are not detectable.
METHODS

1. To monitor for the presence of a gas phase in the pulmonary artery and, in some experiments, the aorta or carotid arteries, use was made of a commercially-available 2 MHz pulsed (or continuous, depending on the subjects) Doppler ultrasound device (Transpect, MedaSonics, Fremont, CA). Standard precordial Doppler ultrasound techniques (Powell et al., 1982) were used similar to those employed at NASA/JSC in previous hypobaric trials (Conkin et al., 1987).

2. To monitor for the presence of cerebral gas microemboli, a 2 MHz pulsed Doppler ultrasound device was employed (Transpect, MedaSonics, Fremont, CA). The MCA was identified on the basis of: (i) anatomic position of the transducer, (ii) depth of the vessel as determined by range gating, and (iii) characteristics of the blood flow signal (Fujoka et al., 1989). "Control" transcranial Doppler signals were obtained from subjects prior to their entrance into the hypobaric chamber.

3. Flow signals in the MCA were expected to be free of gas bubbles when the subjects were resting. Upon flexure of a joint, showers of gas bubbles were detected in the pulmonary artery by means of a precordial Doppler bubble detector in some subjects. These same individuals were checked for the presence of bubbles in the MCA following joint flexure.

4. Gas bubbles in the MCA with a radius equal to or greater than approximately 50 micra were expected to give discrete acoustic reflections. (Spencer, 1990; Powell, unpublished observations). Spencer described these signals as:

(a) transient, less than 0.1 second in duration depending on their position in the velocity/frequency fast Fourier transform (FFT) spec-

trum;
(b) random in position in the cardiac cycle;
(c) greater than 6 dB above the background Doppler flow signal; and
(d) unidirectional.

Smaller gas bubbles could be expected to reveal their presence by an increase in the reflectance of the Doppler signal; this would be seen as brightening of the FFT display on the instrument's screen (Chimowitz et al., 1991).

5. In separate studies not involving decompression, saline contrast echocardiography was performed by rapidly drawing saline back and forth between two syringes in tandem following the addition of a small volume of air to fill the hub of one syringe. This solution was then injected in a bolus through a catheter placed into an antecubital vein. The subject was positioned supine with a slight tilt to the left, and he or she breathed normally. The echocardiograph screen was observed for the appearance of bubbles. If gas traveled into the left heart, a diagnosis of "spontaneous" or "resting" ASD was applied. In the absence at this point of gas bubbles in the left ventricle, a provocation or augmentation maneuver was performed wherein the contrast agent was injected as the subject bore down (Valsalva's maneuver) and then exhaled. This method is standard clinical practice and has been successful in the detection of ASDs (Teague and Sharma, 1991; Lin et al., 1992; Chimowitz et al., 1991).

RESULTS

A. GAS BUBBLES IN THE MCA CIRCULATION

The majority of individuals with even numerous gas bubbles present in the right heart did not have ultrasonically detectable gas bubbles in the systemic arterial circulation.
The number of individuals with neurologic DCS (Type II), presumably from arterial gas bubbles, was approximately what would have been expected from the results of Powell and Spencer (1981) with Doppler-monitored sheep. In these animals, during 86 decompressions resulting in Spencer precordial Grade III or higher, bubbles were detected in the carotid artery in 7 percent with Grade IV precordial bubbles, and in 50 percent with Grade IV+ (it is not known if IV+ is realistically attained in humans under usual conditions). In the human subjects of the present study, 13 had Grade III bubbles or higher, and one (8%) had arterial bubbles.

Of the three people with resting PFOs who participated in the present study, two experienced Spencer Grade IV bubbles. One of these individuals demonstrated arterIALIZation and developed neurological symptoms. The other subject did not give any evidence of right-to-left shunting either by insonation of the left ventricular outflow tract or with the TCD. The third subject did not display a high grade of bubbles according to Spencer’s scheme, but the FFT display “brightened” during his experiment, possibly indicating the presence of a very large number of very small bubbles in the pulmonary artery. Transcranial Doppler monitoring was not performed in this individual. This person developed symptoms of decompression sickness that consisted of skin marbling and orthostatic instability, and the subject received hyperbaric therapy.

A summary of these results is presented in Table I.

**B. NUMBER OF GAS BUBBLES IN THE RIGHT HEART**

The maximum number of gas bubbles in the right heart during decompression is not known, although an estimate can be made.

**1. Gas Loads Following Decompression**

Powell and Spencer (1981) determined from steady-state infusions of gas through a capillary into sheep and by additional deep-diving experiments that the gas content of a Spencer precordial Doppler Grade IV is:

\[
\text{beat } \frac{V_{\text{comp}}}{V_{\text{dec}}^2} = 2.5 \times 10^{-2} \text{ [cc/kg/min]} \times 50 \text{ [kg]} \times 80 \text{ [beats/min]}
\]

\[
\text{beat } \frac{V_{\text{comp}}}{V_{\text{dec}}^2} = 1.6 \times 10^{-2} \text{ [cc/beat]}
\]

**2. Gas Loads Upon Contrast Injection**

These gas volume estimates are derived from the work of Keller et al. (1987) and Sanders et al. (1991) where they estimate the radius of the air-filled microbubbles at 3 micra. We can thus calculate:

\[
V = \frac{4}{3} \pi r^3
\]

\[
V_{\text{microbubble}} \approx 1 \times 10^{-10} \text{ [cc/bubble]}
\]

These investigators estimate that for full opacification of the right ventricle upon B-mode visualization, 0.04 [cc injectate/kg] of fluid containing \(4 \times 10^8\) [air-filled microspheres/cc injectate] are required. This would approximately correspond to the B-mode opacification (or be somewhat greater) seen upon visualization during decompression:

\[
V_{\text{microbubble}} \approx 1 \times 10^{-10} \text{ [cc air/bubb.]}
\]

\[
\times 4 \times 10^8 \text{ [bubbles/cc inject.]}
\]

\[
\times 5 \times 10^{-2} \text{ [cc inject./kg]}
\]

\[
\times 80 \text{ [kg]}
\]

\[
V_{\text{microbubble}} \approx 16 \times 10^{-2} \text{ [cc]}
\]

This volume appears over approximately 16 heart beats. Thus

\[
V_{\text{microbubble}} \approx 16 \times 10^{-2} \text{ [cc]} / 16 \text{ [beats]}
\]

\[
\text{beat } V_{\text{microbubble}} \approx 1 \times 10^{-2} \text{ [cc/beat]}
\]

Thus the injected microspheres (microbubbles) and the decompression bubbles (for a
Grade IV) are approximately equal in volume.

DISCUSSION

1. Earlier Studies

During air injection experiments (per catheter into the jugular vein of sheep) when large $(r = 100-300 \, \mu m)$ bubbles served as the pulmonary embolizing agent, gas bubbles were not detected by perivascular Doppler cuffs on the carotid artery when RVSP was less than 150 percent of pre-injection control (Powell et al., 1980). In studies to achieve these steady-state pressure elevations, air injections were conducted for 10 to 20 minutes. In cases where small microbubbles were infused $(r = 10 \, \mu m - 90 \, \mu m)$, but for short injection periods $(t < 2 \, \text{minutes})$, Doppler-detectable gas was again not found on the systemic arterial side (Butler and Hills, 1979). One could conjecture that a combination of small bubble radius in conjunction with elevation of pulmonary artery pressure act in concert to effect arterialization. Both conditions are necessary and neither alone is sufficient. The very smallest of bubbles $(r < 5 \, \mu m)$ might be expected to dissolve during transpulmonary passage (Meltzer et al., 1980).

A singular contribution of Doppler ultrasonic bubble detectors to our field has been the demonstration that bubbles can appear copiously in the central venous return, but are seen only rarely in the arterial system. Studies of gas separation in two highly perfused organs, kidney and brain, have indicated that these tissues do not readily produce a gas phase following decompression -- even when rather aggressive efforts are undertaken to induce one (Powell and Spencer, 1980). Thus, a highly perfused tissue, such as the brain, seems to be resistant to gas phase formation in all but the severest cases of decompression. Neurologic decompression sickness in the brain could have an origin in arterial gas embolism.

The question of transpulmonic passage of the gas phase was first investigated in rats by Emerson, Hempleman and Lentle (1967); their work indicated that a gas phase could not readily pass the pulmonary barrier under normal physiological conditions. Similar studies by Powell (1971) with rats indicated that arterial bubbles could be found in those subjects which expired, although not all rats with arterial bubbles would necessarily die. Furthermore, the majority of these animal subjects showed no evidence of systemic arterial bubbles following decompressions on profiles known to result only in limb-bend decompression sickness.

It is logical to assume that since venous bubbles appear before arterial bubbles, the source of arterial bubbles is the pulmonary vasculature. It should be stressed here that, in situations where the vena cava is monitored, this vessel will contain a number of gas bubbles before any are noted in the arterial system. In some cases (e.g., viewing of a small field through a microscope), researchers have seen bubbles moving prodromically in an arterial branch when the conjugate venule was bubble-free. The arterial phase did arise from pulmonary arterilization, and an *arterial paradox* does not exist. Arterial gas tensions are thought to closely follow inspired pressures, not be supersaturated, and not produce bubbles. This lack of nucleation was found to be true in sheep decompressed at the rate of 10 fsw/sec (Powell and Spencer, 1982). When Doppler probes were placed around the femoral artery, no gas bubbles were detected even though the supersaturations (from the transit time of blood from lung to leg) were estimated to be 5 ATA at the surface.

In Doppler-monitored sheep, during 86 decompressions in which the animals displayed Spencer Grade III or higher, bubbles were detected in the carotid artery in 7 percent of the subjects displaying Grade IV precordial bubbles, and in 50 percent of those with Grade IV+ (Powell and Spencer, 1980). As Grade IV effects the greatest increase in RVSP, one sus-
pects venous bubbles were arterialized in part by forced passage through A-V shunts or the alveolar capillaries themselves. While Grade IV is not commonly encountered in human divers, it is not as rare an event as one might imagine, especially in hypobaric decompressions or in caisson workers. From the Spencer and Powell studies, it appears that the appearance of Doppler-detectable gas bubbles in the systemic arterial circulation is a rare, but not totally improbable, event; it even occurs in the absence of massive pulmonary vasculature overload (Powell and Spencer, 1980).

Arterialization occurred at definite pressures for Butler and Katz (1988) in dogs, and the mechanism would appear to be straightforward. A rise in RVSP would drive the gas phase through the pulmonary vasculature as seen in a rat study (cf. Powell and Spencer, 1980). However, when other measurements were made with rats as subjects, the results were inconclusive; numerous combinations of RVSP and time of appearance of arterial bubbles were seen. Similar results have also been found in pigs (Vik, et al., 1989).

Cardiac septal defects could be a source of arterial bubbles, although these emboli might be "silent" (produce no symptoms) in most cases. Wilmshurst et al. (1990) found no relationship between type II DCS and the presence of septal defects (3/34 = 24%); curiously, these defects occur in about one quarter of the general population (26/105 = 25%). Similarly, Brubakk and Grip (1981) reported finding asymptomatic arterial bubbles by Doppler devices in ascents from deep diving.

Moon et al. (1991) reported on 90 recreational divers who had suffered decompression sickness (59/90 had neurologic involvement). Echocardiography on these individuals demonstrated that a "resting PFO" (i.e., a Valsalva maneuver was not necessary to provoke the passage of detectable saline contrast bubbles into the left heart) was found in 37% of these stricken divers compared to 10.9% of the controls. The odds ratio was a 4.9-fold risk for neurologic decompression sickness when compared to the controls. They suggested that Valsalva-induced shunts were probably not a factor in the natural history of neurologic DCS. What could not be determined in the studies of Moon et al. is the precordial Doppler bubble grade which occurred during the dives resulting in DCS. The production of such bubbles is, of course, significant if arterialization of bubbles is to occur at all.

In altitude decompressions, the gas loads to the right heart could be expected to be considerably greater than those in diving and thus to pose a larger threat of neurologic DCS. A study reported by Clark and Hayes (1991) examined the prevalence of PFOs in those individuals having encountered Type II DCS during hypobaric training flights. They found 16% (4/24) had a patency demonstrated by saline contrast echocardiography following a Valsalva maneuver; there were no patencies with only spontaneous breathing. They found that controls demonstrated a 5% (9/176) incidence with spontaneous breathing and another 6% (10/176) with Valsalva provocation. They considered the difference not to be statistically significant. The prevalence of PFOs certainly would not explain the origin of the CNS problems in the remaining 84%. Surprisingly, the latencies for symptoms in this study averaged 16 hours with a range of 2 to 21 hours.

The question of the pathophysiology of arterial embolism has been of importance to clinicians with regard to the mechanism of "paradoxical stroke" and its suspected embolic origin. Teague and Sharma (1991) found an incidence of right-to-left shunting of 26% at rest and an additional 15% with Valsalva strain with 2-D echocardiography in stroke patients being evaluated for ASDs. With the addition of TCD, a 41% incidence of ASDs was detected. Lin et al. (1992) compared transthoracic versus transesophageal echocardiography and
reported that both methods possessed an approximately 90% success rate in discovering ASDs. Chimowitz et al. (1991) studied few individuals with TCD (N = 4) but one displayed evidence of numerous microbubbles by an increase in the amplitude of the Doppler audio FFT spectrum; classical single bubble echoes appeared 30 to 60 seconds later. However, ASDs can not be found in all paradoxical stroke patients.

We have not yet been able to identify why one individual who had positive echoes in the left atrium by saline contrast (in the recumbent position) did not also evince bubbles (when lying likewise in the recumbent position) when displaying Grade IV bubbles with lower extremity movements. This individual was checked in the left ventricular outflow tract and in the MCA. As with paradoxical stroke, the presence of right-to-left shunts does not explain the whole problem.

2. CNS Consequences

In general, the involvement of the central nervous system (CNS) in decompression sickness has been considered to be uncommon; less than 10% of individuals presenting with decompression sickness in the U. S. Navy were classified as having CNS, or Type II, decompression sickness. However, deep sea divers with decompression sickness have a high incidence of subtle, subjective complaints such as lethargy, confusion, mental cloudiness, and a general perception that all is not well; this may indicate cerebral involvement. Many of these symptoms have also been experienced by individuals who have undergone a safe decompression, and who have not experienced what classically would have been called frank decompression sickness.

Vaernes, Klove and Ellertsen (1989) noted mild-to-moderate (> 10% impairment) neuropsychological changes in measures of tremor, spatial memory, vigilance, and automatic reactivity in divers having undergone saturation decompression. These subtle effects of decompression were found by Curley et al. (1989) in many cases to be refractory to recompression treatment. This has led to concern regarding the risk for long-term, decompression-induced lesions of the central nervous system in the diving population.

Using injection of \(^{99}\text{Tc}\)-hexamethylpropyleneamine oxime and single positron emission tomography, Adkinson et al. (1989) found perfusion deficits in the cerebral circulation of all human divers one month post an episode of CNS decompression sickness. This was true even when clinical involvement of the brain was absent and only signs of spinal cord lesions were evident. This indicated that Type II decompression sickness is a diffuse, multifocal disorder. Neuropsychological testing has been used to quantify some lesions (Becker, 1984; Kelly and Peters, 1975; Levin, 1975; Peters et al., 1977).

Studies by Gorman et al. (1986, 1987) have shown that gas bubbles in the cerebral arterial circulation could be expected to traverse these capillaries under certain conditions. Cerebral gas distribution is dependent upon the perfusion pressure, and this is an interaction of the arterial blood pressure, cerebrovascular resistance, and intracranial pressure. The relation is complex since the resistance is a function of the blood pressure because the system maintains a relatively constant flow over a range of blood pressures (cerebral autoregulation).

In cerebral gas infusion studies, discrete microbubbles were not seen after the gas entered the arteriolar circulation; rather, coalescence, or fusion, occurred and cylinders of gas formed. Entrapment occurred in vessels when the diameter was reduced to 50 to 200 micra. Transcapillary passage was dependent on systemic blood pressure and embolus length, L. If the embolus length in this vessel was greater than 5,000 micra, blockade was inevitable; if \(L < 500\), blockage never occurred. Intermediate gas bolus lengths (500 < L < 5000 micra) were
found to pass within 3 minutes. These values accord with those of Masurel et al. (1989) who calculated that a bolus would become trapped when its length exceed 10 times its radius.

It is possible to make some estimates from these results. If the volume $V$ of a cylindrical capillary of length $L$ and radius $r$ is given by

$$V = \pi r^2 L,$$

calculation shows the following:

$$V_{500\mu} = 7.7 \times 10^6 [\mu^3],$$
$$V_{5,000\mu} = 7.7 \times 10^6 [\mu^3].$$

With the lower boundary of detectable gas bubble radii as $r = 50$ micra, the volume $V$ of such a bubble can be calculated from $V = (4/3)\pi r^3$ as $3 \times 10^5$ cubic microns. We could determine the number of such gas bubbles needed to fill the 5,000 micron-long capillary and estimate that approximately 260 are needed. Employing Spencer’s (1990) observation that one subject who sustained a post-surgical stroke demonstrated gas emboli in the MCA for 14 seconds, this would arithmetically equate to 18 bubbles/second. This volume is easily detected and is more than was found in severe decompressions in animal (sheep) studies (Powell and Spencer, 1980).

In situations where a Doppler probe was placed over the sagittal sinus (surgically implanted in sheep) gas bubbles were heard just moments after their appearance in the carotid artery (Powell and Spencer, 1980). This would indicate that, in many cases, gas bubbles easily pass through the capillary circulation of the brain (as is true of other tissues as well) since a gas bubble is so highly deformable. The question of a "clinically silent" gas phase may rest with the ability of the systemic arterial blood pressure to force the cylindrical gas emboli through the brain capillaries. Systolic arterial pressure will be a function of, amongst others, the gas load in the right ventricle and its ability to influence cardiac output. (Unfortunately, formed emboli do not possess the same property of deformability.) The transcranial Doppler device (Aaslid, 1986; Aaslid and Lindgaard, 1986; Aaslid et al., 1982; Fujioka et al., 1989) is providing information on this question of the presence of arterial bubbles, and more data will be forthcoming in the near future.

Evidence of the "silent" nature of some arterial gas bubbles comes from observations of Spencer (1990) made with the transcranial Doppler flowmeter at surgery. During carotid endarterectomy, when the arterial wall was invaded, bubble signals could be found in 38% (35/91) of the patients. He notes, "It is clear that not all of the detected emboli signals produced symptoms. Even when many bubble signals occurred, stroke was rare. Also, since visual deficits were never noted postoperatively, even when bubble emboli obviously had passed through the ophthalmic artery, the retina must be relatively unaffected by them." However, these observations in anesthetized individuals must be applied cautiously to awake subjects because of the profound changes in cerebral metabolism and autoregulation that occur during anesthesia.

REFERENCES


ach A. J. and M. M. Matzen, eds., Proceedings, VIII Symposium on Underwater Physiology. Undersea Medical Society, Bethesda, MD.


Primary references:


<table>
<thead>
<tr>
<th>SUBJECT #</th>
<th>MAXIMUM DOPPLER GRADE</th>
<th>TCD Bubbles</th>
<th>SALINE CONTRAST</th>
<th>ECHOCARDIOGRAPHY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AMBULATORY</td>
<td>BEDRESTED</td>
<td>AMB.</td>
<td>BEDREST</td>
</tr>
<tr>
<td>1.</td>
<td>0 (1)</td>
<td>0 (7)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>2.</td>
<td>III (6)</td>
<td>0 (2)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>3.</td>
<td>III (2)</td>
<td>0 (4)</td>
<td>0</td>
<td>.</td>
</tr>
<tr>
<td>4.</td>
<td>IV (15)</td>
<td>IV (3)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5.</td>
<td>0 (3)</td>
<td>0 (10)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>6.</td>
<td>III (4)</td>
<td>II (5)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7.</td>
<td>0 (5)</td>
<td>0 (6)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>8.</td>
<td>IV (7)</td>
<td>Withdrawn from study</td>
<td>+</td>
<td>.</td>
</tr>
<tr>
<td>9.</td>
<td>IV (11)</td>
<td>0 (8)</td>
<td>.</td>
<td>0</td>
</tr>
<tr>
<td>10.</td>
<td>0 (8)</td>
<td>Lost to follow-up</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>11.</td>
<td>0 (10)</td>
<td>0 (9)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>12.</td>
<td>0 (9)</td>
<td>Lost to follow-up</td>
<td>0</td>
<td>.</td>
</tr>
<tr>
<td>13.</td>
<td>III (13)</td>
<td>II (12)</td>
<td>.</td>
<td>0</td>
</tr>
<tr>
<td>14.</td>
<td>IV (12)</td>
<td>0 (13)</td>
<td>0</td>
<td>.</td>
</tr>
<tr>
<td>15.</td>
<td>Lost</td>
<td>0 (14)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>16.</td>
<td>0 (14)</td>
<td>0 (11)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>17.</td>
<td>0 (19)</td>
<td>0 (15)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>18.</td>
<td>0 (19)</td>
<td>0 (16)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>19.</td>
<td>0 (16)</td>
<td>Lost to follow-up</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>20.</td>
<td>III (21)</td>
<td>III (17)</td>
<td>.</td>
<td>0</td>
</tr>
<tr>
<td>21.</td>
<td>Withdrawn</td>
<td>0 (18)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>22.</td>
<td>0 (18)</td>
<td>0 (23)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>23.</td>
<td>IV (20)</td>
<td>0 (22)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>24.</td>
<td>IV (22)</td>
<td>0 (20)</td>
<td>0</td>
<td>.</td>
</tr>
<tr>
<td>25.</td>
<td>IV (24)</td>
<td>II (21)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>26.</td>
<td>0 (23)</td>
<td>0 (24)</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>27.</td>
<td>Withdrawn from the study</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SUMMARY:**

<table>
<thead>
<tr>
<th>Precordial Grades</th>
<th>TCD Bubbles/Subjects:</th>
<th>With Resting PFO</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = 12</td>
<td>0 = 17</td>
<td>0/2</td>
</tr>
<tr>
<td>I = 0</td>
<td>I = 0</td>
<td>1/0</td>
</tr>
<tr>
<td>II = 0</td>
<td>II = 3</td>
<td>0/3</td>
</tr>
<tr>
<td>III = 5</td>
<td>III = 1</td>
<td>0/3</td>
</tr>
<tr>
<td>IV = 7</td>
<td>IV = 1</td>
<td>1/6</td>
</tr>
</tbody>
</table>

12/24 individ. 5/22 individ.

Resting R-L Shunts = 4/15 = 26%