# Size distribution of intravascular air emboli produced by decompression

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Hills BA, Butler BD. Size distribution of intravascular air emboli produced by decompression. Undersea Biomed Res 1981; 8(3):163–170.—Intravascular bubbles formed by decompression have been measured in 7 living dogs to give 14 different determinations of size distribution. Larger bubbles were estimated by the terminal rise velocity technique using the Stokes equation, while smaller bubbles were determined simultaneously, using the Coulter counter. Bubble diameters of 19–700 $\mu$m were recorded, these reaching the venous sinus as showers of several hundred whose mean size tended to increase with post-decompression time. Average diameters were rather smaller than previously recorded from autopsy. The results are discussed as indicating that all venous bubbles were within a size range where they would be filtered out by the lungs unless this organ had been insulted.

air embolism
bubble distribution
decompression sickness
pulmonary embolism

In the early days, decompression sickness was simply attributed to nitrogen bubbles in the blood (1, 2). Later studies of the etiology, however, tended to group symptoms into categories of similar physiological mediation of the basic insult, one of the first classifications to be introduced by the Medical Research Council, London, simply differentiating between local and neurologic manifestations (3). Different mechanisms have been proposed for the various categories of decompression sickness, such as attributing limb bends to the extravascular gas (4, 5) demonstrated so clearly by Boycott et al. (6). However, there still remains a strong interest in intravascular bubbles in view of their potential danger as infarcting agents. While there is little doubt that the category of the less common yet very serious symptoms classified as cerebral decompression sickness can be attributed to arterial gas embolism, this mechanism cannot be ruled out as the basis or factor contributing to the spinal and vestibular categories, also.

Hence, it is most desirable to know as much as possible about the nature of intravascular bubbles as they are produced by decompression—arterial bubbles, if possible, but particularly the large numbers of venous bubbles from which the arterial ones are probably derived. Of particular interest is the size distribution of venous bubbles formed by decompression, since

this may give some insight into their origin and fate. It might also provide valuable information in determining what fraction of venous bubbles should escape entrapment by the lungs because they are smaller than the "cutoff" diameter for filtration by the pulmonary circulation (7).

While Doppler techniques can be used for detection or, in some cases, for counting the bubbles produced by decompression, such monitors are difficult to use as indicators of actual size. Generally, comments on bubble size are derived from autopsies in which decompressed animals are examined following death. Such techniques, however, may not be totally representative of the living state, since the original bubbles may have coalesced during dissection or have formed after death (6).

This study is designed to determine typical bubble size distribution by direct and almost immediate analysis of blood samples taken from the vessels of live dogs at various intervals following decompression. Information obtained from this study is of primary importance in the examination of the complex microembolism process, while the methodology is applicable to subsequent studies of decompression sickness.

## METHODS AND MATERIALS

### Surgical and compression procedures

Seven dogs (18–24 kg) were used in this study. The animals were anesthetized with sodium pentobarbital (30 mg/kg Nembutal, Abbott Laboratories) and intubated to allow for spontaneous respiration. A silastic catheter (Fr. no. 24) was placed in the sinus venarum cavarum from a right venous cutdown. This provided a wide cross section of the vessel from which to take the sample.

The animals were heparinized (15,000 U sodium heparin) and, following a stabilization period, the surgical cradle was placed inside a pressure chamber. The venous catheter was connected to a Teflon-lined, high pressure stopcock valve located on the external wall of the chamber, which allowed for blood withdrawal at depth while the animal remained undisturbed within the chamber.

The chamber was pressurized with air at a rate of 60 ft/min (18.3 m/min). Following a preselected exposure at depth (see Table 1 for exposure times and depths) the animals were decompressed at a rate of 75 ft/min (23 m/min) to a sampling depth of 4 fsw (1.2 msw). This sampling depth was selected to allow blood to flow freely from the sampling catheter with minimal effect on the diameter of any entrained bubbles—approximately 8%, according to Boyle's law.

### Sampling of blood

Immediately post decompression, blood samples were passively withdrawn in 50-ml aliquots via the venous catheter; i.e., blood flowed freely under the pressure gradient without any need to use suction. Thus the hydrostatic pressure of blood exceeded that on the outside, so that no erroneous bubbles could be formed by air entering the sampling system from outside. Sampling periods usually lasted until death, a control sample being taken prior to compression.

The placement of the sampling catheter in the venous sinus meant that bubbles produced systematically were collected from one pooled location. This location was selected for its relevance to pulmonary air embolism, since all bubbles at that site would normally be carried to the pulmonary circulation, where trapping is vital if they are not to enter the arterial circulation.

**TABLE 1**
SIZE DISTRIBUTION OF VENOUS BUBBLES PRODUCED BY DECOMPRESSION IN DOG*

| Dog No. | Weight, kg | Minutes Post Decompression | Exposure, fsw/min | Bubble Diameter Range, $\mu$m |
|---|---|---|---|---|
| 1 | 18.6 | 20 | 160/90 | 103–128 |
| 2 | 24 | 10 | 160/80 | 39–58 |
| 2 | 24 | 20 | 160/80 | 57–61 |
| 2 | 24 | 30 | 160/80 | 30–49 |
| 3 | 22 | 30 | 166/60 | 42–63 |
| 4 | 19 | 20 | 120/180 | 19–50 |
| 5 | 18 | 30 | 160/120 | 31–39 |
| 5 | 18 | 40 | 160/120 | 87–179 |
| 6 | 18 | 5 | 150/150 | 24–32 |
| 6 | 18 | 12 | 150/150 | 26–48 |
| 6 | 18 | 15 | 150/150 | 35–60 |
| 6 | 18 | 23 | 150/150 | 80–159 |
| 6 | 18 | 34 | 150/150 | 52–151 |
| 7 | 18 | 10 | 150/120 | 30–36 |

*Bubbles whose diameters exceeded 180 $\mu$m were measured using terminal rise velocity techniques; they ranged up to 700 $\mu$m in most runs.

Venous bubbles were collected in the sample chamber from the cannula attached to the stopcock valve (see Fig. 1). The sample chamber was filled with heparinized fluid (3 U/ml) in which prefilled sample vials were submerged. Bubbles, along with some trailing blood, rose into the clear fluid column, where size determination was made by use of terminal rise velocity

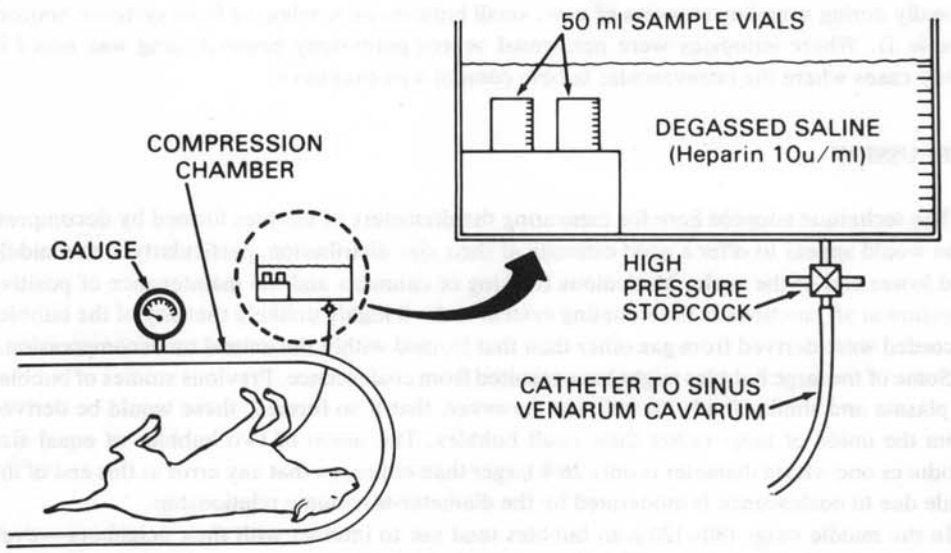


Fig. 1. Schematic of collection method for samples of intravascular bubbles formed following decompression. The catheter passes through the chamber wall to the base of the sample chamber. As bubbles rise into the clear fluid column they are collected in the sample vials for size measurement.

techniques, while a Coulter counter (Coulter Electronics, Hialeah, FL) was used to measure the smaller bubbles from the sample vials.

**Determination of bubble size**

The method of choice for bubble measurement depends on the initial size range. For the larger bubbles (100–200 $\mu$m diam), the terminal rise of a bubble through a static fluid is related to its diameter (d) by the Stokes equation:

$$d^2 = 18\,\nu\eta/\rho \qquad (1)$$

where $\eta$ is the viscosity and $\rho$ is the fluid-air density difference, and $\nu$ is the velocity of the bubble. For smaller bubbles a Coulter counter (Model ZF) was used for sizing and distribution. This method, described previously (7, 8), has a high degree of accuracy ($\pm 0.1$ $\mu$m) with the benefit of an immediate oscillographic display of bubble volume.

The rapidity with which samples were counted and sized enabled determination of distribution ranges before these smaller bubbles could coalesce.

Arterial bubbles were measured in one particular animal from blood samples obtained from the thoracic aorta. Coronary artery bubbles were sized by direct microscopic examinations once the thoracic cage was separated. All bubbles were sized at normal pressure.

## RESULTS

Size distribution of decompression-induced bubbles are presented in Table 1. The larger bubbles observed (> 180 $\mu$m) are described in the referral note and could be largely attributed to coalescence. A single distribution plot for smaller bubbles is depicted in Fig. 2, where the size ranged from 24 to 32 $\mu$m in diam for the 5-min sample. Where the results of several samples are plotted against time (Fig. 3), diameters appear to increase proportionately. Occasionally during sampling showers of new, small bubbles were released from systemic sources (Table 1). Where autopsies were performed severe pulmonary hemorrhaging was noted in many cases where the intravascular bubble content was excessive.

## DISCUSSION

The technique adopted here for measuring the diameters of bubbles formed by decompression would appear to offer a good estimate of their size distribution, particularly at the middle and lower end of the scale. Meticulous flushing of cannulas and the maintenance of positive pressure at all junctions in the sampling system make it highly unlikely that any of the bubbles recorded were derived from gas other than that formed within the animal by decompression.

Some of the large bubbles might have resulted from coalescence. Previous studies of bubbles in plasma and similar fluids (9) indicate, however, that if so formed, these would be derived from the union of large rather than small bubbles. The union of two bubbles of equal size produces one whose diameter is only 26% larger than either, so that any error at this end of the scale due to coalescence is moderated by the diameter-to-volume relationship.

In the middle range (80–120 $\mu$m) bubbles tend not to interact with their neighbors—even upon collision (9). The very small bubbles are unlikely to be the progeny of collision fission of the smaller bubbles (70–90 $\mu$m), in which range this phenomenon has been demonstrated in plasma (9).

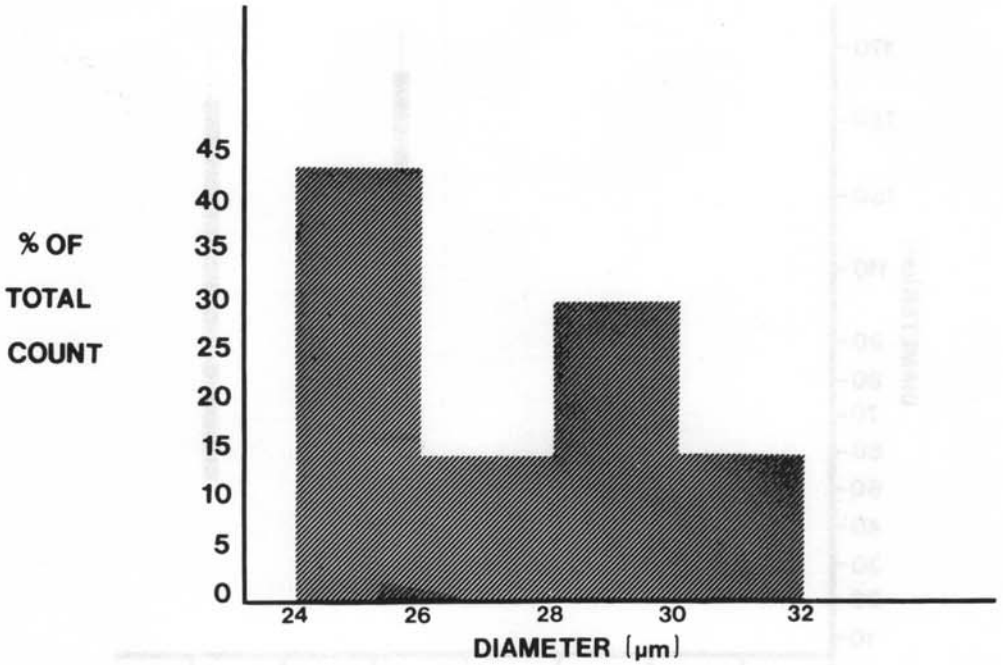


Fig. 2. Size distribution of bubbles taken from the venous sinus 5 min after decompression (dog #6).

In any case, collision fission tends to produce a much different size distribution with a sharp peak around 40 $\mu$m. Thus, it is probably fair to claim that since no outside air enters the sampling system and there is little likelihood of bubbles changing size by collision, the results should offer a good reflection of those actually produced in intravascular sites.

Our findings are in essential agreement with autopsy studies where Gersh (10) found bubbles ranging from 60 to 300 $\mu$m in diam in fatty tissues in both extravascular and intravascular sites. Pulmonary vessels in the guinea pig contained bubbles ranging in diameter from 40 to several hundred micrometers. Gersh and Catchpole (11) observed venous bubbles ranging from 67 to 900 $\mu$m. The rather larger bubble ranges can easily be attributed to the much greater opportunity for gas to coalesce in the autopsy situation. On the other hand, it must be remembered that the decompressions employed in this study were severe.

Knowledge of the size distributions of intravascular bubbles produced in the living state by decompression is particularly desirable in considering their fate. Size is a major factor in determining how far a single bubble will penetrate the bifurcating arterial system supplying any organ. This, as well as the dilation caused by bubbles of varying sizes, has been demonstrated in the cerebral circulation (12).

While arterial bubbles are very serious clinically, a review of the published evidence (13) indicates that, unless caused by an explosive ascent, bubbles occurring during or after decompression are usually observed in the venous circulation before the arterial. This supports the suggestion that arterial bubbles have venous origins, in which case it is most important to consider the effectiveness of the lungs as a bubble trap. If entrapment is simply a matter of filtration, as might be expected, then the factors determining whether venous emboli are trapped or not must include the performance of the pulmonary circulation as a filter and the size distribution of the bubbles presented to it. Studies of the dog lung have shown that if there

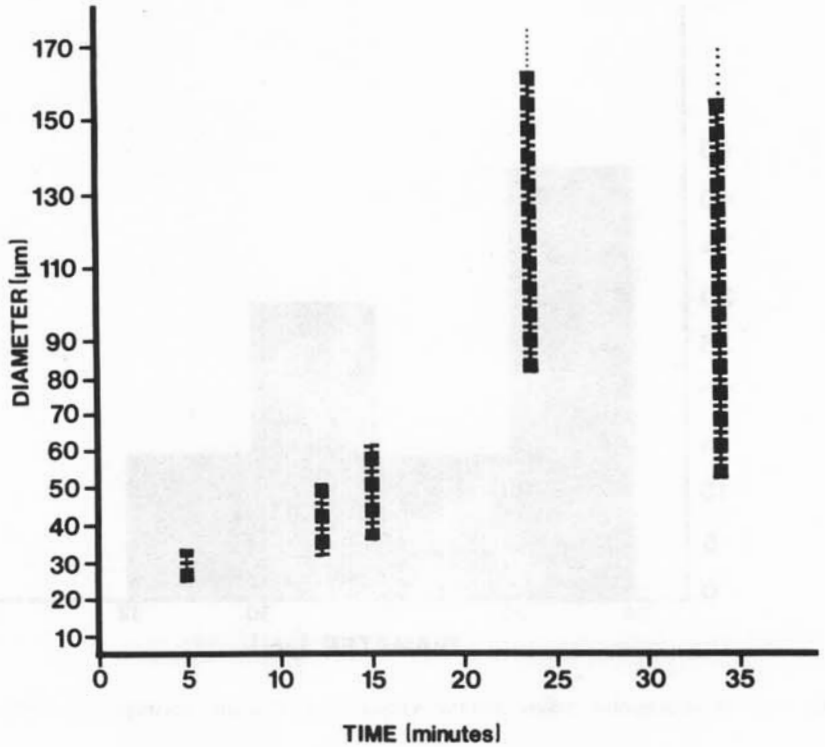


Fig. 3. Size range of venous bubbles taken from dog #6 plotted against post-decompression time.

is any "cutoff" diameter for the size of bubble that the lung will filter, then it is lower than 22 $\mu$m under normal conditions (7). This is particularly interesting in light of the above results in which only one animal produced venous bubbles of lesser diameter and then only just below that size (19 $\mu$m). Hence it is likely that all venous bubbles produced by decompression will be filtered under normal conditions. This does not mean, however, that venous bubbles produced by decompression will remain trapped or continue to be filtered under abnormal conditions such as prevail when pulmonary vasodilators are administered (7) or the lung is insulted with excessive oxygen exposure (13, 14) or by overloading its filtering capacity (7, 15). While the initial removal of bubbles from the pulmonary circulation may be a matter of simple filtration, their retention by the lung may depend on a much more complex set of factors. This is indicated by the delay of up to 30 min (7) in the appearance of bubbles on the venous side of the embolized, insulted lung, i.e., in systemic arterial blood, whatever role pulmonary surfactants might play in facilitating their release (16).

Another feature of the results with venous bubbles is the general increase in average bubble size with post-decompression time; this would seem to be adequately explained on the basis of continued growth following decompression. This increase in size tends to confirm washout studies (17) indicating that the majority of gas in the body as a whole remains in a supersaturated state following decompression—even after decompressions that can produce severe injury. Unfortunately it offers no answer to the really important question (4) concerning when bubbles start to form in the other tissue zones, but this study was not designed to address that issue.

Although not offering a definite answer, the results shed some light on the question of whether the venous bubbles often seen in profusion following decompression form de novo (18) within microvessels into which the gas diffuses, or whether they have extravascular origins and enter the venous system by rupturing endothelium (2). The occasional appearance of a shower might favor the latter on the basis that rupture of the capillary wall—as demonstrated photographically (19)—is a distinct event, whereas bubbles emerging from a continuously nucleating source (such as an imperfection in the wall of a bottle of soda water) tend to be uniform and emerge in a continuous stream. On the other hand it could be argued that each shower represents too many bubbles to be injected into the vascular system by the rupture of just one capillary, whereas a local change in vasomotor tone could cause the release of bubbles formed de novo within a bundle of microvessels (13). Unfortunately the study did not permit fat emboli to be detected to confirm earlier indications (13) that their known appearance following decompression (20) coincided with the appearance of bubbles, as would be predicted if those bubbles were derived from extravascular sites in the fatty tissues where they abound (6, 11).

In conclusion it can be stated that bubbles formed in vivo and removed from the living animal tend to be smaller than the ranges previously recorded on autopsy yet within the range where venous bubbles should be filtered by the lungs under normal conditions.

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Hills BA, Butler BD. La distribution par taille d'emboli gazeux intravasculaires du fait de la décompression. Undersea Biomed Res 1981; 8(3):163–170.—Les bulles intravasculaires qui se forment des suites de la décompression ont été mesurées chez 7 chiens vivants afin de fournir 14 définitions distinctes de la distribution par taille. Les bulles larges ont été évaluées par la méthode de vitesse d'augmentation finale en employant l'équation de Stokes, tandis que les petites bulles ont été définies simultanément en faisant usage du compteur Coulter. Les diamètres de bulle ont été enregistrés de 19 à 700 $\mu$m, ceux-ci ayant atteint le sinus veineux en douches de plusieurs centaines, dont la taille avait tendance à augmenter lors du temps de post-décompression. Les diamètres moyens étaient plutôt inférieurs à ceux enregistrés auparavant à l'autopsie. Ces résultats s'inscrivent dans un cadre où toutes les bulles veineuses étaient comprises dans une gamme de tailles qui leur permettraient d'être filtrées au dehors par les poumons à moins que cet organe n'ait été insulté.

l'embolie gazeuse
la distribution des bulles
la maladie de décompression
l'embolie pulmonaire

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