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Body fat does not affect venous bubble formation after air dives of moderate severity: theory and experiment

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Schellart NA, van Rees Vellinga TP, van Hulst RA. Body fat does not affect venous bubble formation after air dives of moderate severity: theory and experiment. *J Appl Physiol* 114: 602–610, 2013. First published January 10, 2013; doi:10.1152/japplphysiol.00949.2012.—For over a century, studies on body fat (BF) in decompression sickness and venous gas embolism of divers have been inconsistent. A major problem is that age, BF, and maximal oxygen consumption ($\dot{V}O_{2max}$) show high multicollinearity. Using the Bühlmann model with eight parallel compartments, preceded by a blood compartment in series, nitrogen tensions and loads were calculated with a 40 min/3.1 bar (absolute) profile. Compared with Haldanian models, the new model showed a substantial delay in N_2 uptake and (especially) release. One hour after surfacing, an increase of 14–28% in BF resulted in a whole body increase of the N_2 load of 51%, but in only 15% in the blood compartment. This would result in an increase in the bubble grade of only 0.01 Kisman-Masurel (KM) units at the scale near KM = I−. This outcome was tested indirectly by a dry dive simulation (air breathing) with 53 male divers with a small range in age and $\dot{V}O_{2max}$ to suppress multicollinearity. BF was determined with the four-skinfold method. Precordial Doppler bubble grades determined at 40, 80, 120, and 160 min after surfacing were used to calculate the Kisman Integrated Severity Score and were also transformed to the logarithm of the number of bubbles/cm^2 (logB). The highest of the four scores yielded logB = −1.78, equivalent to KM = I−. All statistical outcomes of partial correlations with BF were nonsignificant. These results support the model outcomes. Although this and our previous study suggest that BF does not influence venous gas embolism (Schellart NAM, van Rees Vellinga TP, van Dijk FH, Sterk W. *Aviat Space Environ Med* 83: 951–957, 2012), more studies with different profiles under various conditions are needed to establish whether BF remains (together with age and $\dot{V}O_{2max}$) a basic physical characteristic or will become less important for the medical examination and for risk assessment.

adiposity; Doppler bubble score; deterministic series-parallel model; blood nitrogen tension; delayed nitrogen release

DECOMPRESSION SICKNESS (DCS) is a systemic pathophysiological, but localized, disorder caused by bubbles of inert gas. While breathing air, on depressurization after diving, caisson, and tunneling work, or flying in an unpressurized aircraft, and/or following extravehicular activity from a spacecraft, an excess of nitrogen gas dissolved in tissue and blood during the compression phase may give rise to bubbles, mainly composed of nitrogen. The large, potentially pathological vascular bubbles are predominantly vascular (14). They mainly arise in the venous part of the circulation. When they occur in the arterial system (due to cardiac shunts or via pulmonary vessels), they can block small arteries and capillaries. There they cause acute local hypoxia and thereafter an inflammatory process (1). More details are available in a recent review on decompression illness (40). Large bubbles are mostly found at the venous side [venous gas embolism (VGE)] and can easily be detected in the pulmonary artery by a Doppler technique (30). In the lungs, they release their gas after which they shrink or vanish.

For over a century of medical diving research (4), it remained largely unknown which (and to what extent) demographic factors promote or suppress DCS. Nowadays, it is generally accepted that increasing age stimulates intravascular bubble formation and DCS (3, 6–9, 36, 38), and that a high maximal oxygen consumption ($\dot{V}O_{2max}$) suppresses bubble formation (8, 36). A potential predisposing factor is body fat (BF) (4, 7).

It is generally agreed that a higher content of BF leads to a higher risk for DCS; many researchers consider this relation to be causal (see, e.g., Ref. 3). As nitrogen is five times more soluble in fatty liquid than in aqueous solutions, it is suggested that, during compressed air diving, a high percentage of BF enhances VGE. Due to the longer half time (or half life) of fatty tissue compared with watery tissue to exchange N_2 with blood, N_2 in fatty tissue is released more slowly in blood than in watery tissue. In general, it is surmised that this allows increased evolution and growth of N_2 bubbles in blood in case of more BF compared with less BF.

Results of studies investigating whether or not the amount of BF is causally related to VGE are inconsistent (3, 4, 8, 10, 26, 36). A complicating issue is that the amount of BF is strongly related to age and $\dot{V}O_{2max}$ (e.g., Refs. 7, 36). In a classical animal compressed-air study with a deadly profile, it was noted " . . . that fatness increases the susceptibility to compressed-air illness . . . " (4); however, age and endurance fitness were not considered in this (over one century old) study from Haldane's group. This was in line with incidental earlier observations of tunnel workers (see e.g., Ref. 10). In an extensive longitudinal study (76 years later) the authors suggest " . . . that obesity may be a contributing factor to the occurrence of decompression sickness" (10); however, again, age and endurance fitness were not taken into account. In a large retrospective study (from 1989), the observed age effect was considered to be due to obesity, which was assumed to be an important risk factor (26); $\dot{V}O_{2max}$ was not determined. In recent prospective studies, the VGE-BF relation or VGE-body mass index (BMI) was studied (3, 6–8, 36). In one of them [profile 35 meters of seawater (msw)/25 min, total ascent time 22 min, severity according to $\int P t^{0.5} \cdot dt$ = 149 msw/min$^{0.5}$, open sea, where Pt is pressure times time], the confounding relations of age and $\dot{V}O_{2max}$ with DCS were not accounted for in analysis of the relation between

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BF and VGE (3). However, in another recent VGE study (the same dive as used in Ref. 3), the relations between the three demographic variables have been considered (7). It was indicated that the bubble grade (BG) of VGE is very significantly correlated to age and $\dot{V}O_{2max}$. Although BF also showed a significant correlation with BG, it was not concluded that BF controls BG (7). However, in those studies, no correction was made for (potential) confounding effects. The same applies to a study with very low hyperbarism [≤0.8 bar (g)] and very long exposures (3–48 h, $Pt^{0.5}$ = 220 msw/min$^{0.5}$, dry simulation), investigating the effect of BMI on VGE (6).

In a recent study (20 msw/40 min, total ascent time 9 min, $Pt^{0.5}$ = 132 msw/min$^{0.5}$, open sea), the problem of multicollinearity was reduced by calculating partial correlations (36). It was shown that BF is (probably) not causally related to BG, whereas age and $\dot{V}O_{2max}$ are; however, there was a considerable range in both age and $\dot{V}O_{2max}$. Another limitation was the pooling of data of two (slightly) different profiles, as well as data of a first and identical second dive; therefore, that study does not allow one to draw firm conclusions (36). To avoid the limitations in the setup of that study, now the range in age and $\dot{V}O_{2max}$ was considerably diminished. Also, apart from the effect of the amount of BF, the influence of the thickness of the subiliac fold was studied. The thickness of this fold is considered to be a measure of abdominal fat (37), which makes a large contribution to BF in men and may comprise the majority of BF. Also, abdominal fat is of interest since its metabolism is different from that of other types of fat (e.g., Ref. 28).

Over the last century, the physiology of decompression phenomena has been described by two classes of models: deterministic ones and probabilistic ones (39). Here, we restrict ourselves to the deterministic ones. Among these models, the oldest ones, the most often applied models are those with the tissues presented as independent compartments (no mutual interactions). Each compartment has its own half time of inert gas uptake and release (the Haldanian model), and, in addition, each has its own maximum (M)-value. With the latter extension, introduced by Workman (43) as a protocol to develop dive tables, the Haldanian model was evolved to the (deterministic) neo-Haldanian model. Other types of deterministic models are those with a number of compartments arranged in series, such as the Defense and Civil Institute of Environmental Medicine (DCIEM) model (31). In Ref. 39, a review can be found on the characteristics of deterministic models and the probabilistic models. In the latter models, which can also be used for table construction, the yes-or-no occurrence of DCS with a given dive profile is probabilistically calculated. In both classes of models, various types have been described (16, 39), and most models are also applicable to gas-mixture diving.

Since our only and exclusive aim is to calculate the N_2 tensions in compartments, the deterministic approach was chosen since it relies on a sufficient number of compartments. These compartments are thought to represent, in some nondefinable way, the body with its tissues. By assigning the compartments, albeit somewhat arbitrarily, to tissues, the compartments can also be assigned a volume. With these assignments, estimates can be made of N_2 tensions and N_2 loads after decompression. With compressed air as breathing gas, the only inert gas of relevance is nitrogen. Since the inert nature of O_2 is probably not present due to its small partial pressure (at most 0.65 bar, Ref. 33), we did not consider O_2 as an inert gas to calculate compartment inert-gas tensions. Hence, the calculations were restricted to N_2.

In the present study, the half times of the neo-Haldanian Bühlmann model, being the basis of decompression tables and many dive computer algorithms (19), are used to calculate N_2 tensions.

In the Haldanian decompression theory (e.g., Refs. 5, 19, 39), the blood, as a separate theoretical compartment preceding the parallel compartments (the theoretical tissues of the body), is ignored (at least quantitatively). The rationale for this is its assumed very short (quasi) half time compared with compartments with a half time of ~5–640 min (5, 39). As an exception, the shortest half time of only 2.5 min attributed to a parallel blood compartment has been used by manufacturers of dive computers. In addition, it was implicitly assumed that the N_2 throughput of the pulmonary-circulatory system is not a limiting factor for uploading and unloading the compartments.

One of the compartments presents fatty tissue, which volume has a large intersubject variation. The question as to whether or not fat divers produce more intravenous bubbles can possibly be solved when the blood is involved as a compartment preceding the parallel compartments of the Haldane model. Using such series-parallel models, the aim is to make a quantitative prediction about the (possibly) higher postdive N_2 tensions in the blood of a fat subject compared with a lean subject. These higher tensions are assumed to produce higher VGE grades. With experimental VGE data (obtained with different percentages of BF), the theoretical prediction can be tested indirectly. Details and performance of some series-parallel models are described in the first part of MATERIALS AND METHODS section.

MATERIAL AND METHODS

Theory and Models

Classical compartment paradigm: model 1. In decompression theory, loading and unloading of the compartments with a square dive can be described by a convex and concave exponential curve, respectively. The underlying physical model is a linear time-invariant system of the first order with an integrating behavior and is described by a first-order linear differential equation. In fluid dynamics, its analog is a system with a resistance to which the flow is subjected and a compliance of the wall of the tube through which the current flows. The electrical analog is a network with a resistance (R) and a capacity (C). For purposes of clarity, we describe the various models from the point of view of electrical analogs and for briefness' sake described in Laplace notation. The input signals (ambient N_2 pressure of the dive profile) and output signals (N_2 tensions of the compartments) have the dimensions of electric potential.

A square dive with an infinite fast descent and ascent can be described as a positive step, [i.e., the increment of inspired partial pressure of N_2 (P_{N_2})], followed after bottom time with a negative step of the same size (decrease of inspired P_{N_2} to surface level). The response of the system (i.e., the change of the P_{N_2} in the compartment) is the superposition of the two sequential step responses. The unit step response is $S(t) = \mathcal{L}^{-1}\{\tau^{-1}/s(s + \tau^{-1})\} = \int h(t) = 1 - e^{-t/\tau}$, where t is time; $\mathcal{L}$ is Laplace transformation; $\tau = RC$ the time constant (= $T_{half}/\ln 2$, where T_{half} is the half time of the compartment); $s = j\omega$, the imaginary angular frequency; and $h(t)$ is the unit-impulse response. A stop is introduced by a negative step of smaller size followed by a small step of, e.g., −3 msw. In fact, the descent and ascent speeds are finite (here: 15 msw/min). The response to a slope (in the dive profile) is the integral of the step response $[\mathcal{L}^{-1}\{\tau^{-1}/s^2(s + \tau^{-1})\} = \int(1 - e^{-t/\tau})dt = t - \tau(1 - e^{-t/\tau})]$. With this elementary approach, the response of any

compartment with known half time can be calculated for any multilevel dive by using the superposition principle for the input and output signal. In practice, it is often more convenient to perform the calculation piecewise (descent, isopression phase, etc.). Then, with any change of depth, the calculated tension before the change is used as the initial value of the new calculation.

This theory is used to calculate the tension of 8 of the 16 compartments of Bühlmanns ZH-L16 decompression table (5), with half times of 5–635 min. In addition to half times, compartment volumes are also needed to calculate N_2 loads (see below). With 16 compartments, attributing a realistic set of 16 volumes is not possible. Therefore, 16 compartments are not a refinement leading to more reliable results. In this and subsequent models, the small effect of the bubbles on the hemodynamics affecting perfusion is ignored. (Total bubble volume is very small compared with blood volume.) A refinement would be to take into account the effects of the oxygen window; this window is dependent on O_2 consumption per compartment, which, however, is not known. Apart from being infeasible, any refinement will barely affect differences between the lean and fat subject.

Table 1 presents the half times and the (more or less) arbitrarily chosen volumes and tissue types attributed to the compartments numbered 1 to 8 (based on Refs. 2, 5, and 27) of a hypothetical lean man. For a hypothetical fat man, *compartment 6* is 23.4 liters (28% fat), and his whole body is 83 liters. All other values are the same for the lean and fat subjects.

Since *model 1* lacks the blood compartment, it is unable to answer the question whether or not obese divers would have a higher BG than lean divers.

A series-parallel model with independent behavior of compartments: model 2. In this model, a blood compartment (including the airways) precedes the parallel compartments. From a xenon diffusion study of the airways-alveoli blood system with xenon in the inspired gas (25), the (quasi-)half time of this system was estimated. Using Graham's law, N_2 half time was calculated as 38 s. The parallel compartments are considered to comprise a perfusion and a diffusion part (39, 42). In the present study, we use the perfusion component only to comprise the pure capillary bed of the parallel compartment; this resulted in an estimated half time of 30 s. The half time and volume of the blood compartment of the lean and fat subjects are considered to be the same. It should be noted that, during physical inactivity, about all of the whole blood volume passes the lungs in approximately 1 min. Without the eight parallel compartments in series with the blood compartment, the half time of 30 s implies that the blood compartment is saturated and desaturated within 4 min.

In the Haldanian approach, the compartments are independent from each other; they do not charge each other. With a preceding blood compartment with an infinite small output impedance (basically unlimited current or flow), the eight parallel compartments still behave independently, but are subjected to the transfer characteristic of the blood compartment. This means that increase and decrease of N_2 tension of the parallel compartments is slightly delayed. The unit-step response $S(t)$ of a parallel compartment is:

$$S(t) = \mathfrak{L}^{-1}\left\{s^{-1} \cdot H_{\text{blood}}(s) \cdot H_i(S)\right\} = (1 - e^{-t/\tau}) * h_i(t) \qquad (1)$$

where $H_{\text{blood}}(s)$ and $H_i(s)$ are the transfer characteristics of the blood and parallel compartment i, respectively, with $H(s) = 1/(\tau s + 1) = 1/(RCs + 1)$, * is the convolution operator, and h_i is the unit impulse function of the ith compartment.

Like *model 1*, *model 2* also cannot be used because N_2 tensions of the fat compartment of the lean and fat divers show an identical behavior. Pairwise (fat and lean), the same holds for all other compartments.

A series-parallel model with dependent behavior of compartments: model 3. In this model, the eight parallel compartments in series with the blood compartment are no longer independent, since, during uploading, they all compete for the same N_2 flow supplied by the blood compartment. In terms of linear systems theory, the output impedance of the blood compartment is not low compared with the input impedances of the eight parallel compartments to which it is coupled. This model is in most agreement with the physiology. In contrast to *model 2*, the N_2 flow to a parallel compartment is dependent not only on its impedance, but also on the impedances of the other parallel compartments. This causes a flow limitation in the blood compartment, resulting in saturation and desaturation of the blood compartment, which takes much longer than 4 min.

Figure 1 shows the electric analog of the whole system. $P_{N_2\ \text{ambient}}$ is ambient P_{N_2}, which is the input signal of the system, $P_{N_2\ \text{blood}}$ (blood P_{N_2}), and $P_{N_2\ 1}$ to $P_{N_2\ 8}$ are the nine output signals of P_{N_2}. To calculate the tensions, the figure shows that (in contrast to *models 1* and *2*) knowing the values of the time constants is not sufficient. The numerical values of the nine individual R and C values are also required.

The transfer characteristic $H^3(s)$ (superscript 3 denotes *model 3*) of this linear ninth order system with $P^3_{N_2\ \text{blood}}$ as output is:

$$H^3_{N_2\ \text{blood}}(s) = \frac{Z_{/\!/}}{R_{N_2\ \text{blood}} + Z_{/\!/}} = \frac{H_1(s) \cdot H_2(s) \cdot \ldots H_8(s)}{\sum_{i=0}^{9} c_i \cdot s^i} \qquad (2)$$

$$1/Z_{/\!/} = C_{N_2\ \text{blood}} s + 1/Z\{H_1(s)\} + \ldots\ldots 1/Z\{H_8(s)\}$$

$$\text{and } c_i = f_i(R, C, R_1, \ldots R_8, C_1, \ldots C_8)$$

where Z is impedance, $R_{N_2\ \text{blood}}$ is blood N_2 resistance, c_i is a constant of compartment i, f_i is function of the ith compartment, $C_{N_2\ \text{blood}}$ is blood N_2 capacity, and where $H^3(s)$ comprises a denominator with as roots nine real poles and a nominator with as roots eight real zeros (thus, one less), as qualitative network theory prescribes. The equation

Table 1. *Half-times and volumes of compartments and N_2 loads and N_2 load ratios of the fat and lean subject 1 h after surfacing*

				N_2 Load Relative to Surface			
				Model 1		*Model 4*	
No.	Compartment	T_{half}, min	Volume, liter	Lean, ml	Fat/Lean	Lean, ml	Fat/Lean
	Blood	0.5	5			2.3	1.15
1	Neural tissue, heart	5	2	0.0	1.0	1.0	1.13
2	Lung	12.5	1	0.2	1.0	1.1	1.03
3	Liver	27	3	5.0	1.0	8.6	0.97
4	Muscle active	54.3	24	89.0	1.0	89.5	0.96
5	Muscle inactive, intestines, skin	109	13	41.6	1.0	39.3	0.96
6	Fat	187	9.7	24.0	2.4	105	2.31
7	Bone, tendons	305	4	7.9	1.0	6.0	0.96
8	Bone	635	8	12.5	1.0	6.3	0.96
	Sum blood and // compartments		69.7	180	1.18	258	1.51

T_{half}, half time of compartments; fat/lean, ratio of fat to lean.

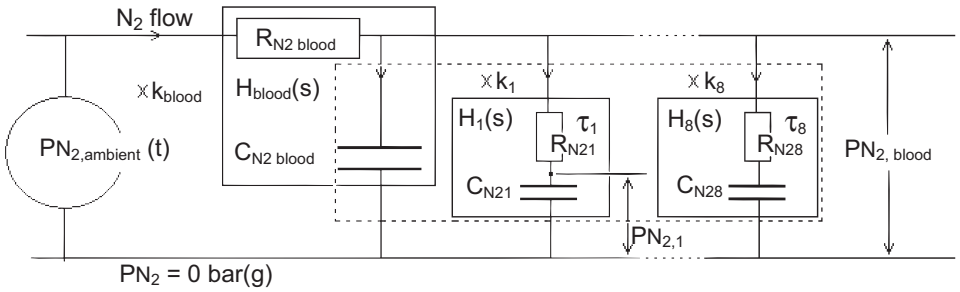

Fig. 1. Analog of the blood compartment with (in series) the 8 parallel compartments 1–8. Pressures are shown as gauge (g) pressures (relative to surface). Factors k account for the compartment volume. The dashed line indicates $Z_{//}$ of *Eq. 2*. See MATERIALS AND METHODS for definitions of terms.

can be solved with analytic mathematics, but only with a computer-aided analytic equation solver. With pilot calculations using Mathematica (Wolfram Research, Champaign, IL), we found 3,228 coefficients in the description of the denominator of $H^3_{N_2\,blood}(s)$. After fracture decomposition to solve the equation and backward transformation to the time domain, the unit-step response $S(t)$ of the blood compartment was found; this comprised nine exponentials:

$$S^3_{N_2\,blood}(t) = 1 - \sum_{j=1}^{9} a_j e^{-t/\tau_j} \text{ with } \sum_{1}^{9} a_j = 1 \qquad (3)$$

The constants a_j and τ_j are real polynomials of the underlying nine R values and nine C values.

In physiological physics, several models are available to calculate time constants of the compartments. Some rely on perfusion and others on a mixed perfusion-diffusion approach (e.g., Refs. 39, 42). Unfortunately, in those studies, the equations of the time constants could not be transformed to time constants comprising the product of a R and C with known numerical values.

To calculate N_2 loads of the compartments, their volumes are needed. Because time constants are material constants, $H(s)$ does not take compartment volumes into account. Volumes can be accounted for by introducing k (an integer) parallel compartments of each original compartment with k proportional to the compartment volume (see Fig. 1) (for the fat compartment 5k). This complication plus the fact that the values of R and C are unknown was the rationale to abandon the analytic approach of *model 3*. Therefore, we decided on a simple heuristic, numeric approach, which was sufficient for our purposes, but still based on the principle of *model 3*.

Model 3 approximated by a recurrent numerical procedure: model 4. To estimate the delayed on- and off-gassing of the blood compartment due to the release (ascent and isopression phase) into and re-uptake (ascent and time after surfacing) from the eight parallel compartments, a numerical approximation of *model 3* was constructed. It was based on the difference between the $N_{2\,i}$ loads at time t and time $t+1$ in the parallel compartments. Each minute, the decrease or increase of blood tension, $P^4_{N_2\,blood}(t)$, was calculated from the release or re-uptake by the blood compartment given by the above difference. The change of $P^4_{N_2\,blood}(t)$ was found by applying Henry's law (from volume to tension) for the summed change of loads of the parallel compartments.

The procedure was as follows. At time $t = 1$ min after the start of the descent, from $P_{N_2\,i}$ calculated with *model 2* the dissolved gas mass [in liter with a pressure of 1 bar (l_{1bar})] in each of the parallel compartments was calculated according to Henry's law (volume/volume notation):

$$V_{N_2\,i\,1bar} = \alpha \cdot P_{N_2\,i} \cdot V_i(l_{1bar}) \qquad (4)$$

where $V_{N_2\,i\,1bar}$ is the dissolved volume of nitrogen, reduced to 1 bar and 37°C, and α is the Bunsen solubility coefficient (liter gas/liter liquid). Blood has a solubility coefficient of 0.0127 $l_{N_2\,1bar}$/l at 37.3°C (15, 41). On the basis of Ref. 41, we assumed that watery tissue has more or less the same α as blood. Nitrogen is 5.15 times more soluble in olive oil than in blood. Although adipose tissue is for ~95% fatty substance, the convention is followed that absorption of the whole fatty tissue is five times that of blood.

Resuming the calculations, $P_{N_2\,i}$ at $t = 2$ was calculated from its previous value with blood pressure in model 4 (P^4_{blood}) at $t = 1$ as its temporary asymptote (driving force). Then, with the new loads at $t = 2$ in the parallel compartments, the increase in load from $t = 1$ to $t = 2$ was summed for all eight compartments, and Henry's law was applied from volume to tension, yielding change in pressure (ΔP). Next, P^4_{blood} at $t = 2$ was calculated from P^4_{blood} at $t = 1$, and ΔP was subtracted since the blood compartment supplied the load increase of the parallel compartments. Then the cycle started again with the calculation of $P_{N_2\,i}$ at $t = 3$. The cycles were repeated for all 1-min samples of the profile, as well as those after surfacing.

Experimental Methods

Subjects and experimental study design. The study was approved by the Ethic Committee of the Medical Faculty of the University of Amsterdam, and by the Surgeon General and Superintendent of Diving of the Netherlands Royal Navy. All subjects signed an informed consent and were informed about the tests by means of a scenario. The experiments conformed to the standards of the Declaration of Helsinki (2011) and to Dutch law on medical scientific research on humans (World Health Organization, 1998, 2012).

A total of 53 male divers (21 divers of the Netherlands Royal Navy, 3 commercial divers, and 29 recreational divers) volunteered to participate in the study. Fitness to dive and experience were established by a medical examination according to the Navy protocol (similar to the NATO protocol) and a questionnaire. The examination took place several weeks (range 1–12 wk) before the experimental session. The recreational divers were preselected based on answers to a questionnaire about dive experience (number of years diving and total number of open-water dives), age, height, and body weight (for BMI), and the numbers of hours per week spent on endurance sport to estimate $\dot{V}O_{2max}$ (based on a model with age, BMI, and hours of endurance sport; Ref. 28). Women and smokers were excluded from the study. After selection, these recreational divers were included for the medical examination. All subjects who passed the medical examination were not allowed to dive 48 h before the dive simulation (to avoid the repetition effect), should not perform endurance sport [which might diminish VGE (11)], and should not use any stimulating drugs for (at least) 1 day before the examination. To obtain standardized measurements, the subjects fasted the night before (from 10 PM). After awakening, at least 2 h before the experimental session, they consumed one glass of water or tea, and 1 h before the session one glass of water or tea and a few prepared slices of bread, in accordance with their corrected ideal body weight (28).

The divers performed a simulated dry 40-min just-decompression dive on air to 21 msw with compression and decompression paces of 15 msw/min and with a 5-min stop at 3 msw, in accordance with the DCIEM tables ($\int P t^{0.5} \cdot dt = 132$ msw/min$^{0.5}$). The dive was performed in the dry compartment of the dive simulator (Medusa, Haux, Germany) of the Royal Navy. During bottom time, the subjects performed 10 blocks of 3.5 min of light to moderate exercise while seated. These

exercises comprised scheduled repeated movements of head, hands, arms, trunk, legs, and feet, made according to the instructions of a dive supervisor, who was also in the hyperbaric chamber. The exercises were performed to mimic swimming and moderately light physical labor.

During the isopression phase, at rest, the subjects (wearing t-shirt and shorts) would be close to thermal equilibrium, since the chamber temperature was 24.7–26.4°C (depending on the season) and was stable in the isopression phase (within ~0.1°C).

Measurements

VGE measurements. The extent of VGE was measured four times, i.e., at 40, 80, 120, and 160 min (as averages) after surfacing time. The VGE measurements were performed precordially at the left third intercostal space with a 2.5-MHz continuous-wave Doppler (DBM9008) with an array probe bubble detector (Techno Scientific, Toronto, Canada). All measurements were performed by the same Doppler technician [T. van Rees Vellinga, certified by Defence R&D Canada (DRDC), Toronto].

One Doppler session (lasting almost 5 min) consisted of four measurements. The first was made with the subject standing at rest, and the remaining three immediately after a deep knee bend (flex). The Doppler sounds were digitally recorded on a personal computer. The recordings were scored blinded by a Doppler expert of DRDC (Toronto, Canada), with BG expressed in Kisman-Masurel (KM) units (30). The highest score after the knee bends was used for further analysis.

Age, BF, BMI, and $\dot{V}O_{2max}$. During the medical examination, $\dot{V}O_{2max}$ was calculated by a maximal test with ergometry and gas analysis. The load of the ergometer (Excalibur Sport, Lode, Groningen, the Netherlands) was stepwise increased. (During the first minute the body weight in kg as wattage, and every subsequent minute an increase of 25% of the weight.) For inclusion, $\dot{V}O_{2max}$ was restricted to the range 35–52 $ml \cdot kg^{-1} \cdot min^{-1}$, resulting in a maximum/minimum factor of 1.5. Without restriction of $\dot{V}O_{2max}$ and age, this factor of recreational divers is 3–4 (8, 36).

Age was expressed in years (accuracy in days). All subjects were aged 40–50 yr; on average, this is higher than the average age of professional and recreational divers. The rationale to select this age range was that older divers have a higher level of bubble stress (e.g., Ref. 7).

To determine BMI (kg/m^2), the subjects wore only underwear and had bare feet. Weight (kg) and height (m) were measured with an accuracy to 1 and 3 decimal places, respectively.

After the first Doppler measurement, BF (in %; recorded with an accuracy to 1 decimal place) was determined with the four-skinfolds method (12). This simple and long-established method has also been used in studies of the DCS-BF relation (10, 26) and appeared to be sufficiently precise for our study (21, 23, 32). There were no limitations for BF.

Analysis of Measurements

To allow parametric statistics, the ordinal KM scores were transformed to a numerical scale: the number of bubbles per centimeter squared (according to Table 10.3.8 of Ref. 30), as used in earlier studies (13, 18, 34, 36). However, the direct use of bubble counts can be inappropriate, since they show considerable deviation between subjects, which results in domination of high counts in the statistical analysis (the outlier problem). Therefore, we used the logarithm of the bubble count (logB) (34, 36). (The rationale for applying logB is discussed in Ref. 35.) For KM = 0 logB = −3 is adopted (e.g., Ref. 34).

For analysis, the four logB values of the KM scores (the largest of the four) and the logarithm of the Kisman Integrated Severity Score (KISS, a measure of multiple KM scores over time) were used (20, 30).

Statistical Analysis

As numeric dependent variables, logB and logKISS were used in parametric statistics. The main methods were calculation of the Pearson binary correlation coefficient R and the Pearson partial correlation $\rho_{xy,\,ab,\,\ldots}$, where a, b, ... are the correcting (or controlling) variables (24). P values <0.05, tested double-sided (Student's t-test), were considered statistically significant. Correlations were calculated with SPSS version 16.0.

RESULTS

Model 1 and Model 2

The loads of *model 1* and *model 2* are almost identical. In *model 2*, the action of the blood compartment on the tensions of the parallel compartments can be described by a latency. This is because $T_{\text{half blood}} << T_{\text{half } i}$. The latency can be approximated by $d = \pi T_{\text{half blood}}/2\ln 2$ [from $d\varphi(\omega)/d\omega$ at $\omega = 0$, where $\varphi(\omega)$ is the phase characteristic of $H_{\text{blood}}(j\omega)$]. For $T_{\text{half blood}} = 0.5$ min, d is 68 s, the time shift between the curves of *model 1* and *model 2*, illustrated with *compartment 1* in Fig. 2. The latency is also the reason why the tensions of fast compartments in Fig. 2 do not decrease immediately after the start of decompression.

One hour after surfacing, the N_2 load of the fat compartment (lean subject; *model 2*) is 83% of the amount at the start of decompression, whereas for *model 4* this is 90%. However, the load with *model 4* is 27% less than that of *model 2*, due to the delayed transport.

Model 3

In *model 3*, uploading and unloading of the blood compartment is delayed compared with *model 2*, as indicated by *Eq. 3*. This is due to the second term ($j = 2$) and (to a smaller extent) to the third term. Explorative calculations showed that the coefficients of the remaining terms are too small to produce any effect. The uploading and unloading of the parallel compartments are also delayed, since $P_{N_2\,i}$ is the convolution of $S^3_{N_2\,\text{blood}}(t)$ (by approximation the first 3 terms of *Eq. 3*) with $h_i(t)$, the impulse response of compartment i.

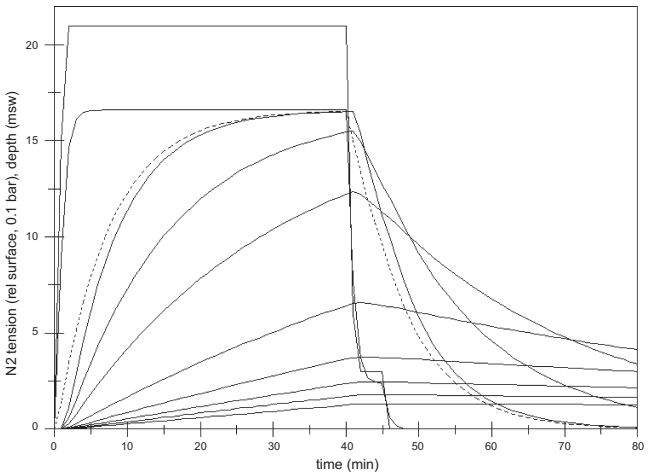

Fig. 2. Nitrogen tensions of the blood and 8 parallel compartments of *model 2*. *Top* curve; profile, followed by tension of blood compartment. The dashed curve is the *model 1* curve for *compartment 1*. Below the dashed curve are the curves of the 8 parallel compartments (*top* one is *compartment 1*, etc.). msw, Meters of seawater.

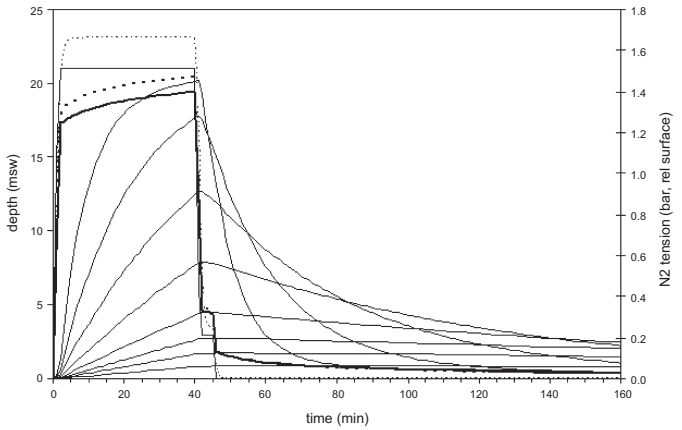

Fig. 3. Nitrogen tension of the compartments in *model 4*. Curves from *top* to *bottom*: dotted-dashed curve, blood N_2 tension of *model 1*; solid line, profile; dashed thick curve, blood N_2 tension of the lean subject; solid thick curve, blood N_2 tension of the fat subject, N_2 tension of the parallel *compartment 1*, etc. The profile has its axis on the *left*, and the tensions are on the *right* side.

Model 4

Figure 4 shows the eight compartment tensions and $P_{N_2\,blood}^4$ of the lean and fat subject. Table 1 gives the N_2 loads of all compartments of the lean subject at the end of the isopressure phase. The fat-to-lean ratio of the loads is increased compared with *model 1*.

From $t = 0$ to the time of decompression (infinite descent pace), $P_{N_2\,blood}^4(t)$ is by approximation:

$$P_{N_2\,blood}^4(t) = 1.60\left[1 - (0.47 \times 2^{-t/0.72} + 0.53 \times 2^{-t/47})\right]\text{bar (rel surface)} \quad (5)$$

with standard error of estimate of 0.0017. The first term has a time constant that is ~50% higher than the half time of the blood compartment. Both terms contribute almost equally, thus accounting for the large delay in the on-gassing of the blood compartment that lasts for many hours (Fig. 3). This emphasizes the considerable influence of the restricted flow through the blood compartment. The delay appeared to be mainly caused by *compartments 4–6*, which have the highest load (Fig. 4). These compartments (assuming that they comprise muscle and fatty tissue) release 5–100 times more than the other compartments.

With a 5-min stop at 3 msw, the effect of off-gassing is considerable for the blood. This is supposed to result in a strong reduction of VGE bubble stress, but for other compartments the decease is much smaller or even nil.

After surfacing, the relative contribution of fat increases slowly, as can also be concluded from Fig. 4. From 86 min after surfacing, the fat compartment has the highest load of all compartments. For the fat subject, at 60 min after surfacing, the fat compartment comprises 62% of the total body load (for the lean subject 41%), whereas, at the start of decompression, this is 40% (for the lean subject 22%). One hour after surfacing, an increase of 14–28% in BF resulted in a whole body increase of the N_2 load of 51%, but in only 15% in the blood compartment.

Figure 4 shows that the N_2 loads of the lean and fat subject are very similar (thick solid curve and dashed thick curve, respectively); the difference is negligible (*left* lower dotted and thin solid curve, respectively).

For VGE, it is not the N_2 load of the body or of the fat compartment but the release into the blood that is the relevant parameter, since that increases the blood N_2 tension, being the driving force for bubble growth. One hour after surfacing, the fat-to-lean ratio of $P_{N_2\,blood}^4$ was 1.15, and in the interval from surfacing until 80 min after surfacing the fat subject has (on average) a 9% higher $P_{N_2\,blood}^4$.

Demography of the Subjects

The basic values of the demographic characteristics are given in Table 2. The distribution of age, $\dot{V}O_{2max}$, BF, and the subiliac fold was (multivariate) normal. BF values were 5 units lower than the Caucasian age-matched mean, and $\dot{V}O_{2max}$ was supranormal (10 units) after taking age into account (22, 27). Age showed no significant partial correlation with $\dot{V}O_{2max}$ or with BF, whereas $\dot{V}O_{2max}$ and BF were correlated ($\rho = -0.41$, $P = 0.02$).

No case of DCS was observed or reported by the divers.

VGE Scores, Log Bubble Counts, and BF

The logB values calculated from the VGE scores at 40, 80, 120, and 180 min are 1.26 ± 0.17, 1.20 ± 0.16, 0.87 ± 0.12, and 0.73 ± 0.10 (means ± SE), respectively. The latter two are significantly lower than the former two (all P values <0.0009, paired Student's t-test). Table 2 gives the primary statistics of the highest of the scores obtained at 40, 80, 120, and 180 min. Figure 5 presents scatter plots of the four KM scores vs. BF. At 120 and 160 min after surfacing, scores higher than KM = 1 were rare. No significant correlations (R and ρ) between BF and the log bubble counts of KM1 to KM4 were found (very large P values). The most relevant data are the largest of the four logB values (shown in Table 2 with the demographics). Its partial correlation (control variables age and $\dot{V}O_{2max}$) with BF was not significant ($P = 0.50$). Also with logKISS, no significant partial correlation coefficient was found ($P = 0.51$). Similar results were found for the thickness of the subiliac fold.

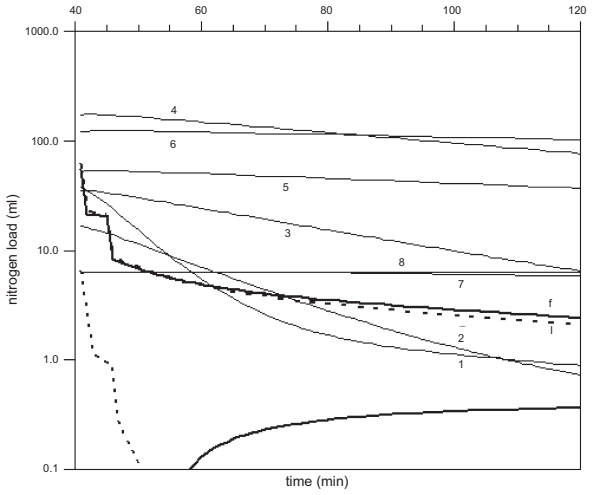

Fig. 4. Total nitrogen loads of the 8 compartments (numbered) of the lean subject, and of the blood compartment of the lean (l) and fat (f) subject. The lowest, thick curve gives the N_2 load fat minus lean. The difference of lean minus fat (sign reversal) is depicted on the *left* (dashed vertical curve).

Table 2. *Demography and values of logB and logKISS*

	Age, yr	$\dot{V}O_{2max}$, ml·kg^{-1}·min^{-1}	Body Fat, %	Subiliac Fold, mm	logB	logKISS
Mean	45.9	42.5	21.0	12.9	−1.78	−0.71
Median	46.0	41.7	21.3	12.0	−1.31	−0.58
Range	40.0–50.9	34.4–52.8	13.4–28.9	5.0–37	−3 to +1	−2.00 to +1.82
SD	3.31	5.68	3.77	6.5	1.29	1.37

$\dot{V}O_{2max}$, maximal oxygen consumption; logB, log of the no. bubbles/cm^2; KISS, Kisman Integrated Severity Score.

DISCUSSION

General Observations

Calculation of the N_2 tension of the blood compartment from its half time and from the changing N_2 loads of the parallel compartments is the basis and the theoretical newness of this study. The model uses the half times of the ZH-L16 decompression table. Small and mostly even moderate changes of volumes and half times (up to 25%, also for the blood compartment) of the linear series-parallel model produced similar outcomes. Hence, half times and compartment volumes are far from critical. The same holds for $T_{half\ blood}$; doubling gives only some slower transport and slightly smaller fat-to-lean ratios. The delayed gas release appears to be an intrinsic property of decompression physiology, as described in various earlier studies (e.g., Refs. 16, 18). Delayed dissolved gas transport has been described for a three-compartment parallel model with mutual asymmetric interactions (16), a model that is inappropriate to calculate blood tensions compared with our models.

The experimental novelty of our approach is the restricted age and $\dot{V}O_{2max}$, which practically eliminated the collinearity between BF and the demographic parameters of age and $\dot{V}O_{2max}$. BF appeared not to influence VGE.

Theoretical Study

With an increase from 14 to 28% BF, the 9% increase of $P^4_{N_2\ blood}$ (from 0 to 60 min after surfacing) will increase the bubble volume by 9%, assuming proportionality between the blood N_2 tension and bubble volume. This will result in (at most) a 9% increase in detectable bubbles. Ignoring that the KM scale is ordinal, this difference yields ~0.01 KM units. In fact, measurement shows that the mean logB (highest of the four) is −1.78 (no. of bubbles/cm^2 = 0.017), which is equivalent to a BG slightly less than I−. Taking into account that, in a group of divers, the KM grades range 3 or 4 units, the difference of 0.01 KM unit is negligible.

Increasing the length of the isopression phase will increase the fat-to-lean ratio of $P^4_{N_2\ blood}$ after surfacing. In the extreme case, for a hypothetical saturation dive (with an N_2 enriched mixture), this ratio becomes 1.4 (0- to 60-min interval after surfacing). This would finally result in a BG of the fat diver of (about) an additional 1/8 KM units. To make this difference in logB significant, a study including about 500 saturation divers is needed. This theoretical example suggests that, for many types of exposures, BF is irrelevant on the basis of the model. From Fig. 3, it can be seen that all compartments have a delayed washout. Although remaining tensions are low, this may give rise to a longer period of gas uptake by existing bubbles. Especially for the fast compartments, e.g., the neural tissue, this is a disadvantage.

Washout is always, to some extent, delayed by, e.g., pulmonary physiology and bubble formation (e.g., Ref. 5). Proportional lengthening of all nine half times after surfacing is a time transformation that does not change the conclusions. Selective lengthening does change the ratios of and differences between lean and fat. Therefore, in the model, we introduced a lengthening of 20% of the half times of *compartments 1–5* and that of the blood compartment. Besides the minor effect on the tensions, visible in a tension-time diagram, the change in loads is minuscule, such that, in Fig. 4, these changes are practically invisible. This again demonstrates the robustness of *model 4*.

Experimental Study

It was found that, 40–80 min after surfacing, VGE is maximal, as also found theoretically. Between 80 and 120 min, VGE decreased sharply. In addition to the lack of an effect of total BF, also abdominal fat does not affect VGE. That neither age nor $\dot{V}O_{2max}$ showed a significant correlation with BGs is attributed to their small range, which is three to four times

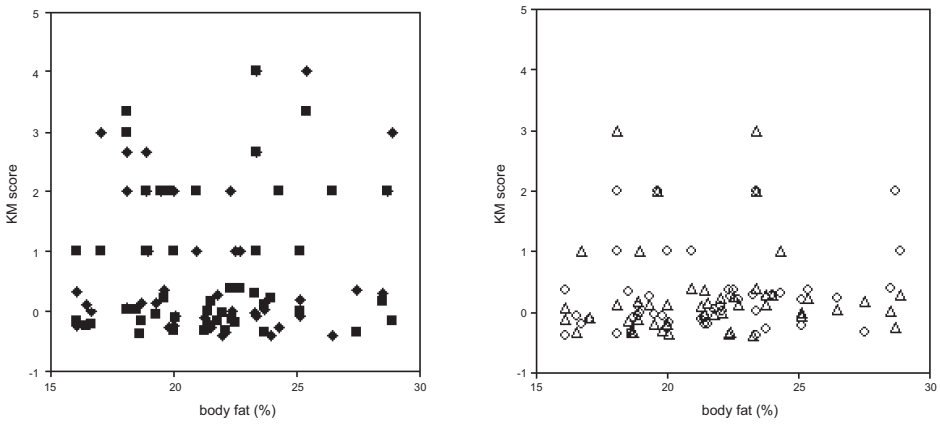

Fig. 5. The four Kisman-Masurel (KM) scores, KM1 (diamonds, *left*), KM2 (squares, *left*), KM3 (triangles, *right*), and KM4 (circles, *right*), measured at 40, 80, 120, and 160 min after surfacing, respectively, vs. body fat. For all scores with KM = 0, a random number between −0.4 and 0.4 was added to distinguish them from neighboring data points. Spearman correlation coefficients of body fat and KM scores were not significant.

smaller than in similar studies (e.g., Ref. 8). Although $\dot{V}O_{2max}$ and fat were negatively correlated, the confounding effect of $\dot{V}O_{2max}$ is practically eliminated, and the outcome of the partial correlation between BF and logB can be considered as not contaminated. A multivariable linear regression (with BF and $\dot{V}O_{2max}$ as independent variables) and logKISS yielded nonsignificant coefficients and a variance inflation factor of 1.8, indicating practically no collinearity.

Professional vs. Recreational Divers

The present study included both types of divers to obtain a sufficiently large sample. Although the recreational divers had 1.3% more fat and were 1.2 yr younger, the differences were not significant. Their $\dot{V}O_{2max}$ is 2.7 points lower, tending to significance. However, all correlations of the subgroups showed nonsignificant outcomes, similar as for the whole group. The recreational divers made 570 ± 473 (mean ± SD) dives over a period of 13 ± 6.9 yr. We conclude that, for the aim of the present study, the professional and recreational divers can be considered as a homogeneous group.

Choice of Times of BG Measurement

Since unloading of the fat compartment takes several hours, we were interested in BGs over a period of ~3 h. Peaking of BG is possibly later the longer the dive (due to the increasing importance of slow tissue). Peaking slightly before 40 min has only been found for a short, deep dive (ca. 38 min, Ref. 3). Therefore 40, 80, 120, and 160 min after surfacing were chosen as measurement times. VGE is highest during the first 1.5 h after surfacing, as found in other studies. This means that the influence of BF on bubble growth after this time period is further diminished.

Effect of Exercise

During the isopression phase, since the subjects were exercising (almost without interruption), almost 100% of the voluntary muscles were active, and not about 80% as suggested in Table 1. It is estimated that O_2 consumption during the isopression phase was ~25 $ml \cdot min^{-1} \cdot kg^{-1}$. This implies that most of the circulation is directed to the voluntary muscles, with a circulation time of ~30 s (5, 27). Therefore, the T_{half} of 54.3 min of *compartment 4* (active muscles) mentioned in Table 1 is supposed to be much shorter, possibly by a factor of about 2 (not exercising is ~12 $ml \cdot min^{-1} \cdot kg^{-1}$, Ref. 27). A similar change applies (in part) for *compartment 5*. *Compartment 4* will start decompression closer to saturation. As a result, the majority (in a lean subject) or almost the majority (in a fat subject) of total body N_2 load resides in the muscles. During and after the decompression phase, the majority of the muscle compartment is close to rest, resulting in the half time of *compartment 5*. Therefore, in Fig. 3, *curve 4* should be shifted a factor 2 upward, and, after the start of the ascent, it should coincide with *curve 5* and obtain the slope of the latter. Consequently, the muscle N_2 load dominates the fat N_2 load. The final result is that the relative difference of the 9% of $P_{N_2\,blood}^4$ of the lean and fat subject shows a strong decrease, resulting in a nil difference in VGE.

Conclusions

The new series-parallel model, linear and intrinsic symmetric, suggests that the rate of nitrogen release (or that of another inert gas) from the parallel compartments takes longer compared with the classical Haldanian model. The theoretical analysis indicates that the original large difference in N_2 load of the fat compartment between the lean and fat diver is reduced to a very small difference in N_2 tension of the blood compartment and will finally be reduced to a negligible difference in VGE BG. Moreover, the profile hardly influences the relative tension difference. This suggests that the classical explanation of the influence of BF on VGE and DCS probably does not appear to be valid. The model outcome is in line with the analysis of our experimental data showing that BF does not affect VGE BG.

The analyses of the data sets of two other studies produced the same results: the study by Schellart et al. (36) with an open water just-decompression dive, and (in this latter study) a reanalysis of the data from the study of Carturan et al. (8) obtained with a close-to-heavy decompression dive. However, although these profiles have severities (estimated by the $Pt^{0.5}$ model, see Introduction) that cover a great part of recreational and Navy dives on air, they do not cover the whole theoretical profile space. For instance, extreme decompression dives and saturation dives may behave differently, despite the model predictions.

The above-mentioned studies (8, 36) and those of others (see Introduction) show that age and $\dot{V}O_{2max}$ are relevant predisposing factors. They also showed that, for air dives with low and moderate severity, BF is a strongly correlated covariable. To reassess the role of BF, more studies with different profiles under various conditions are needed. Then it will become clear whether BF can still be used as a basic physical characteristic (together with the predisposing factors age and $\dot{V}O_{2max}$), or whether BF will become less important for the medical examination and for DCS risk assessment.

However, also when future studies confirm our results, BF will remain (to some extent) an indicator for VGE stress and DCS risk. Diving medicine institutions can then decide whether they will set up a double or triple criterion, based on a combination of age, $\dot{V}O_{2max}$, and BF, to pass the examination for recreational and professional divers.

We have no arguments to exclude women from the conclusions.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: N.A.S., T.P.v.R.V., and R.A.v.H. conception and design of research; N.A.S. and T.P.v.R.V. performed experiments; N.A.S. analyzed data; N.A.S. interpreted results of experiments; N.A.S. prepared figures; N.A.S. drafted manuscript; N.A.S., T.P.v.R.V., and R.A.v.H. edited and revised manuscript; N.A.S., T.P.v.R.V., and R.A.v.H. approved final version of manuscript.

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