Journal of
Biodiversity & Endangered Species

Windberger UB et al., J Biodivers Endanger Species 2015, 3:1
DOI: 10.4172/2332-2543.1000149

Research article Open Access

Blood Rheology in Cape Fur Seals and Bottlenose Dolphins: Implications for Muscle Perfusion

Ursula B Windberger[1*], **Roland Auer**[2] **and Malcolm J Smale**[3]

[1]*Department of Biomedical Research, Medical University of Vienna, Austria*

[2]*Biomedical Research Center, University of Pretoria, South Africa*

[3]*Port Elizabeth Museum at Bayworld, and Department of Zoology, Nelson Mandela Metropolitan University, Port Elizabeth, South Africa*

[*]**Corresponding author:** Ursula B Windberger, Medical University of Vienna, Waehringerguertel, Vienna, Austria, Tel: +43(0)1-4040052230; E-mail: ursula.windberger@meduniwien.ac.at

Received date: January 08, 2015; **Accepted date:** March 06, 2015; **Published date:** March 13, 2015

Abstract

Blood O_2-storage in diving animals is increased by great numbers of large erythrocytes which carry enhanced hemoglobin contents. In seal and dolphin, resting hemato (HCT) and/or red blood cell (RBC) indices were elevated (HCT: seal: 50 (47/51); dolphin: 45/50); MCH: seal: 35.8 (34.4/37.3); dolphin: 41/40); MCHC: seal: 33.9 (33.4/36.0); dolphin: 35.6/36.6), and RBC volume was increased (seal: 101 (99/110); dolphin: 115/110 fL) compared to terrestrial animals and man. However, WBV increases in parallel with the HCT. In seals, we therefore calculated the range in which the desired HCT effect is not weakened by an increase of WBV; we plotted the theoretical oxygen transport capacity ($WBV*HCT^{-1}$) against the HCT. A quadratic regression showed that the resting HCT was higher than the optimal HCT value (at $11.6s^{-1}$: 31%; $40.5s^{-1}$: 37%; $267s^{-1}$: 45%; all: $p<0.05$). This may facilitate blood stasis during a dive, when HCT is further increased through splenic release of RBC. Flow curves of seals showed shear thinning (11.6/500: seal: 1.98 (1.87/2.11), indicating that the blood texture changes with shear rates. RBC deformability in seals was pronounced (elongation index (ectacytometry) at 60Pa: females: 32, 29; males: 24, 24), but aggregability was low (aggregation indices M_0: 3.15 (1.6/4.8); M_1: 13.3 (8.7/18.8)), and therefore intermediate regarding Weddell seal (high aggregability) and ringed seal (nil). Considering the importance of aggregability on the cell free layer width in arterioles, feeding of RBC into subsequent vessels at bifurcations may be enhanced.

Keywords: Blood viscosity; Hemorheology; RBC aggregation; RBC deformability; Marine mammals; Seal; Dolphin

Introduction

Evolutionary theory would predict that any mechanism that extends the aerobic dive limit of marine animals [1] should be selected. This can principally be achieved by the enhancement of the body O_2 stores, by optimization of their utilization, and by the reduction of the cellular O_2 demand during the dive. Apart from the specialized respiratory and myogenic O_2 storage capacity in the body, blood O_2 storage connects the two others by the species-specific O_2-affinity of hemoglobin [2], and by the continuous movement of blood through the vasculature. The rate of this movement depends on hemodynamic and geometric cardiovascular variables, and on the fluidity of blood and plasma. The fluidity of blood itself is influenced by quantitative and qualitative properties of Red Blood Cells (RBC) and the plasma composition, which in combination determine Whole Blood Viscosity (WBV). The viscosity of blood is low due to the ability of RBC to change their shape according to the hemodynamic forces and by the rotation of the phospholipid membrane around the cytoplasm. The ability of mammalian RBC to aggregate and deform essentially provide the viscoelastic behavior of blood, although plasma colloids may play some role as well [3]. In-vitro flow curves of blood show a higher WBV value at low shear rate ($<10\ s^{-1}$), and a decrease of WBV when shear rates are raised ($>100\ s^{-1}$). Thus, thinning of blood occurs with the shear, and as a result, blood viscosity will be different in the vascular compartments. Shear thinning depends on the extent of RBC aggregation and disaggregation at low and intermediate shear rates, and on the RBC deformation at higher shear rates. The species-specificity of this property is surprising, and is assumed to be a fingerprint for a certain species [4].

The diving response is characterized by an increase of peripheral resistance and a reduction in heart rate [5]. Since venous return matches the peripheral resistance, cardiac output is decreased and enables a physiologic systemic perfusion pressure [6]. The reduction of cardiac output is associated with the reduction of muscle perfusion. For instance, in seals during forced submersion, muscle perfusion is close to nil, and heart rate and cardiac output are low. During sleep apnoea of animals on the surface, muscle perfusion is present, although reduced, and heart rate is not that low compared to forced submersion [7,8]. Complete isolation of the muscles from the circulation to prevent lactate washout during forced or prolonged dives would sequester a certain blood volume in the entire vascular network of those muscles for a period of several minutes. This raises the question of whether hemorheological parameters play a role in the generation of blood stasis. At the same shear stress in a given vascular segment, blood stasis could occur earlier when RBC aggregation and haematocrit are increased.

Our in-vitro measurements of blood from Cape fur seals, *Arctocephalus pusillus puscillus* indicate that blood stasis may even be facilitated in specific vascular regions, which would foster RBC sequestering in areas of low flow during a prolonged dive. As stated recently [9], the advantage of increasing the volume of O_2 that can be

carried by the blood may more critical to the animal than the efficiency at which it can be delivered.

Materials and Methods

Animals

Blood was collected during routine health checks from 2 bottlenose dolphins (*Tursiops aduncus*, 1 male, 1 female) and 6 Cape fur seals (3 male, 3 female) kept in the Bayworld aquarium, Port Elizabeth, Republic of South Africa. Four of these seals (seal 1, 3, 5, 6) had been rescued as black pups from a beach when they were washed off the breeding colony in Algoa Bay during storms. The other two seals (seal 2 and 4) were born in captivity. The two dolphins were second and third generation born in captivity, respectively. Blood was withdrawn by vacutainer systems from the flipper veins of seals and tail fluke veins of dolphins. Blood was put into EDTA-tubes and placed on ice. All the animals, except one of the dolphins, were clinically healthy at the time of the blood collection. One of the dolphins showed clinical signs of gastritis. However, the routine blood chemistry was within the reference range.

Laboratory measurements

Hematology was performed by Advia 2120 Haematology Analyser (Siemens, Berlin, Germany) to obtain red blood cell count (RCC, in cells $10^9 \mu L^{-1}$), Mean Cellular Volume (MCV, in fL), mean cellular hemoglobin concentration (MCHC, in g dL^{-1}), and White Blood Cell Count (WCC, in cells $10^6 \mu L^{-1}$). A routine blood chemistry profile was performed to check the health status (NEXT/VETEX and ACE Alera; Alfa Wassermann B.V., Woerden, The Netherlands). Hematocrit (HCT) was measured by centrifugation (JOUAN "Hema C"-centrifuge, Hawksley & Sons, West Sussex, Great Britain).

The hemorheological measurements included Whole Blood Viscosity (WBV, in mPa.s), Plasma Viscosity (PV, in mPa.s), RBC aggregation (aggregation indices: M_0, M_1) and RBC deformability (Elongation Index: EI).

WBV (η) was analyzed by the strain-controlled Physica MCR301 rheometer (Paar, Graz, Austria). Shear rates between 11.6 and 500 s^{-1} were adjusted for data processing. Isothermal runs at 37°C were conducted with a logarithmic shear rate ramp. To show the shear thinning of blood, the ratio of WBV at the lowest (η11.6) and the highest measured shear rate (η500) was calculated [10].

PV was analyzed by the rolling ball viscometer AMVn (Paar, Graz, Austria). Plasma was tested at a 60° capillary angle (capillary diameter 0.9 mm; stainless steel ball diameter 0.794 mm) at 37°C.

RBC aggregation was analyzed by the Myrenne Aggregometer MA1 (Myrenne, Roetgen, Germany). Aggregation indices M_0 and M_1 were obtained for each sample (native HCT) at room temperature (22°C). At least five readings were taken for each individual value to obtain mean values for M_0 and M_1.

RBC deformability was checked by laser diffractometry by the Rheodyn SS (Myrenne, Roetgen, Germany) at room temperature (22°C). The device displays an Elongation Index (EI), expressed as percentual elongation, at eight different shear stresses (τ) between 0.3 and 60 Pa.

Experimental protocol

Due to technical reasons, measurements were performed at two time points. Hematology and blood chemistry was performed on each time point from each individual. Hemorheological measurements needed a larger amount of blood and were split for both time points. At the first time point, RBC deformability and plasma viscosity was checked (only 4 seals were present at that time) at Bayworld immediately after withdrawal of blood. At the second time point, RBC aggregability was checked at Bayworld, but for the measurement of whole blood viscosity, seal blood had to be transported from Port Elizabeth to Johannesburg by airfreight. The samples were transported in insulated bags below 10°C and reached the laboratory after a six hour time interval. The blood was checked for hemolysis or clot and suspicious samples were removed. All measurements were finished within 12 hours following the withdrawal of blood.

To measure the range, at which HCT is "optimal", blood from the seals was centrifuged for HCT adjustment. Concentrated blood cells and autologous plasma were carefully re-mixed to obtain HCT values between 15% and 94%, and WBV was analyzed subsequently.

Statistical analysis

Descriptive statistics were performed in the SPSS software (PASW Statistics 17) showing median, 25%, and 75% percentile of parameters in seals. For the 2 dolphins the individual values are presented.

Theoretical oxygen transport capacity through the formula $HCT \cdot WBV^{-1}$ was calculated in seals only. $HCT \cdot WBV^{-1}$ was plotted on the linear axis against its respective HCT value. A regression analysis was used to test whether HCT has quadratic influence on $HCT \cdot WBV^{-1}$.

Results and Discussion

In comparison to terrestrial mammals [11,12,13], HCT was elevated in our Cape fur seals and bottlenose dolphins. The high volume of the RBC allows higher intracellular O_2 concentrations.

	Cape fur seal	Bottlenose dolphin
HCT (in %)	50 (47/51)	45 / 50
RCC (in10^9cells/μL)	5.2 (5.0/5.4)	3.72 / 4.36
MCV (in fL)	101 (99/110)	115 / 110
MCH (in pg)	35.8 (34.4/37.3)	41.0 / 40.3
MCHC (in g/dL)	33.9 (33.4/36.0)	35.6 / 36.6
TP (in g/dL)	7.8 (7.5/8.1)	7.4 /7.9
PV (in mPa.s)	1.32 (1.27/1.33)	1.19 / 1.22
M_0	3.15 (1.6/4.8)	4.1 / 3.8
M_1	13.3 (8.7/18.8)	15.1 / 16.5
η11.6 / η500	1.98 (1.87/2.11)	-

Table 1: Hematology, total protein concentration as well as aggregation indices (M_0, M_1) at native hematocrit and plasma viscosity (PV) of Cape fur seal and bottlenose dolphin. The viscosity ratio (η11.6 / η500) shows the degree of shear thinning of blood. Data of

seals are expressed as median and 25% and 75% percentile in parentheses

The concentration of hemoglobin in the RBC was also increased (Table 1). This result is in accordance with other findings [5,14]. Compared to other seals [9], hematological values were low. Our captive seals could not experience the high level of exercise undertaken by free-living animals. Generally, they lived at the surface with short dives and ad libitum swimming in shallow water (<3 m deep). Since the spleen releases RBC during the dive [15], the life style of our animals - being at the surface or swimming in shallow water - might have resulted in a constant sequestering of RBC in the spleen. The two seals born in captivity (seal 2, seal 4) exhibited no difference in HCT, MCV, MCH, and MCHC compared to the other four seals that were born in the wild. Possibly, the phenotype of the animals in regard to hematology had not yet changed. There is the possibility that the HCT in free living Cape fur seal increases during prolonged deep dives. As an increase of HCT impacts blood fluidity through the viscosity increase. The transport of O_2 to the organs may be limited as a result.

To estimate the significance of the elevated HCT value on blood flow, we used the following approach [16]: We calculated the theoretical oxygen transport capacity of blood - which is described in a simplified way by the HCT to WBV ratio out of a series of WBV-measurements at incremental HCT values. When $HCT.WBV^{-1}$ is put on a linear y-axis, it generally yields a curve concave to the HCT-axis (on the linear x-axis). The maximum of this curve reflects a theoretical value indicating a range where the benefit of RBC in the bloodstream is not reversed by a concomitant increase of viscosity. Due to the availability of larger amounts of blood, which are necessary for the measurements, we performed them for seals only. Regression coefficients R^2 were: 0.476 for 11.6 s^{-1} (significance of coefficient: $p<0.05$), 0.612 for 40.5 s^{-1} ($p<0.01$), and 0.704 for 267 s^{-1} ($p<0.001$). At 40.5 s^{-1} and 267 s^{-1} the regression curve had its maximum at 37.5% and 45% HCT, which was lower than the resting HCT of the animals. At 11.6 s^{-1}, this maximum shifted further towards a lower HCT (31%) (Figure 1).This approach, however, has limitations. For instance, the formula cannot predict O_2-delivery, since hemoglobin O_2-affinity and –dissociation, or RBC transit time in the microvasculature [17] are not included. Furthermore, the formula is not designed to consider vascular geometries or hemodynamic parameters. It merely focuses on the two main parameters that estimate oxygen transport on the blood level. Despite that, we think it may be useful to suggest the range in which the HCT of an individual may be "optimal". The application of this formula on our data denotes that the resting HCT value in our seals is higher than its theoretical "optimal" range up to shear rates, normally postulated in peripheral arteries [18]. It can be seen from the tests that resting HCT moves towards its "optimal" range, when the WBV at higher shear rates (267 s^{-1}) is entered into the formula. This would indicate that O_2 transport is suboptimal in vascular regions with low shear rate, and that higher intravascular shear rates are needed to facilitate blood flow. Low shear rates are present in large vessels at low blood flow. Typical low flow vessels are the post capillary venules and the capacitance vessels. During submergence further low flow vessels should be present in association with the individual diving response of the animal. The second finding was that RBC flexibility in our Cape fur seals was comparably high, which should facilitate capillary transit of the RBC. Comparison is provided in (Figure 2) with species-specific data obtained in our laboratory [19,20]. This result is, however, weakened by the low number of measurements in seals. RBC deformability in seals may be sex dependent: female seals had higher EI than the male individuals. However, data are too few to make a definite conclusion.

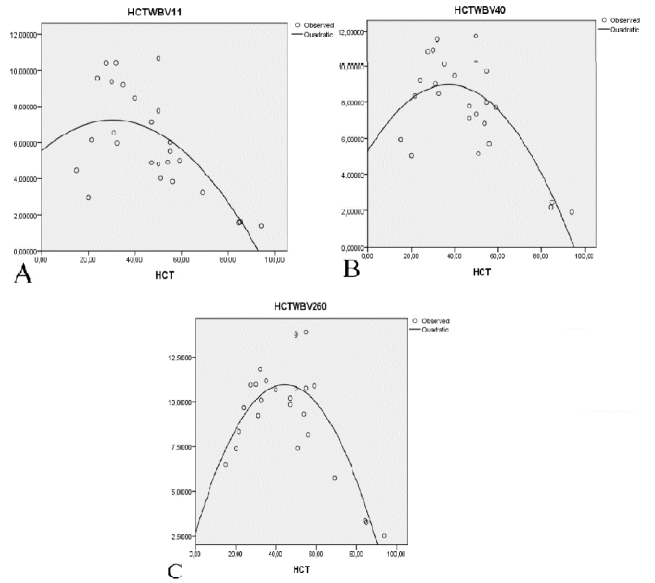

Figure 1: Theoretical "optimal HCT" plots ($HCT.WBV^{-1}$) on the y-axis versus HCT on the x-axis) of Cape fur seal at various shear rates (A: 11.6 s^{-1}; B: 40.5 s^{-1}; C: 267s^{-1}). Theoretical "optimal" hematocrit increases with the shear rate. Regression coefficients R^2 were 0.48 for 11.6 s^{-1} ($p<0.05$), 0.61 for 40.5 s^{-1} ($p<0.01$), and 0.70 for 267 s^{-1} ($p<0.001$)

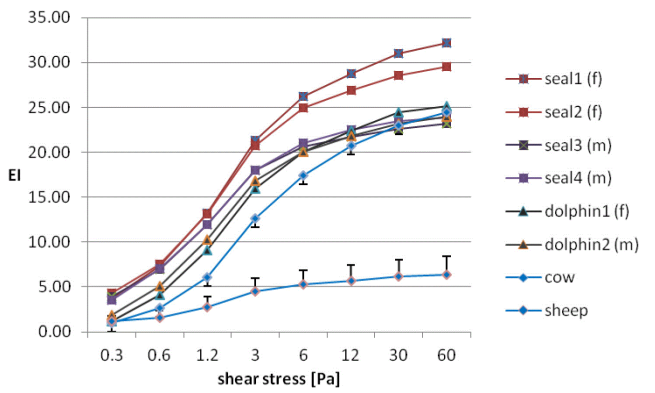

Figure 2: Elongation index vs. shear stress curves in 4 seals (2 male, 2 females; seals 2 and seal 4 were born in captivity), and 2 dolphins (1 male, 1 female) measured by Laser diffractometry. At shear stresses above 3 Pa, RBC elongation in the 2 female seals is higher than in the 2 male seals. References values are from sheep and cow, two terrestrial species with remarkable differences in RBC deformability. Although cow RBC show good elongation during shear, the indices of seals and dolphins were even higher. This is also the result of the large volume of seal and dolphin RBC

The third finding was that RBC aggregability in Cape fur seals was in a low range, compared to other mammals [4]. Compared to other pinnipeds, it was much lower than in Weddell seal [14], but higher

than in ringed seal [21]. Instead, RBC aggregability of our seals had a comparable quality to dogs. Flow curves of native seal blood indicated that blood had its typical shear thinning property, although RBC aggregability was low (Figure 3). There may be no gender difference in blood viscosity. Generally, we are aware that our results are rather tentative rather than conclusive due to the small number of animals available. It has to be kept in mind that body mass, body movement, and dive duration of Cape fur seal are quite different from most phocid seals [22]. Therefore the species cannot be directly compared. In the two bottlenose dolphins, RBC aggregability was comparable to our seals.

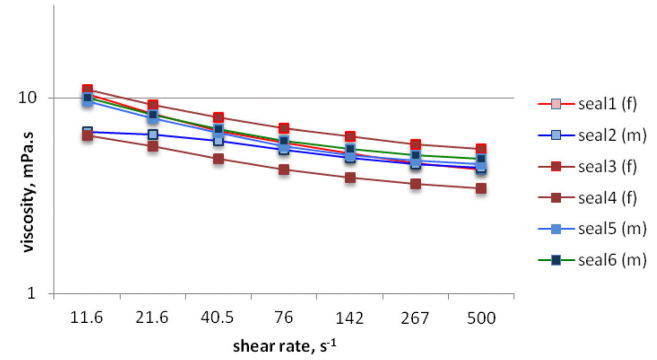

Figure 3: Flow curves of whole blood at native HCT in Cape fur seals (3 male, 3 female) at shear rates between 11.6 and 500 s^{-1}. The typical shear thinning behavior of blood is generated by the reversible formation and break-up of RBC aggregates when the shear rates change. Seal 2 and 4 were born in captivity in contrast to the other four seals

These findings may have implications on blood flow. First, blood stasis may be facilitated, because the resting HCT was higher than its suggested optimal value. Second, capillary passage is not reduced through RBC rigidity. Third, endothelial shear stress as the result of the low RBC aggregability may be enhanced. This point will be discussed below.

RBC aggregability is associated with NO bioavailability and vascular diameter. At physiologic conditions, which imply a regular endothelial cell phenotype, vessel diameters are adjusted by the shear stress stimulus [23,24]. It is important for the organisms that shear stress is controlled in order to prevent pro-atherogenic cell phenotypes [25]. Experimental studies showed that eNOS expression and phosphorylation in endothelial cells could be modulated by changes in RBC aggregation [26]. There is a cell free zone at the marginal fluid layers in arteries that shows spatial variations with the blood flow partitioning at bifurcations [27,28]. The association of that Cell Free layer Width (CFLW) with the shear stress response of the endothelial cell has been evidenced [29]. The CFLW is the result of the bulk blood structure in a specific vessel and associated with RBC aggregability. If RBC aggregation is present, the axial migration of RBC reduces the viscosity on the outer fluid layers. Through this shear stress reduction the NO production in the endothelial cell is diminished. In our Cape fur seals, RBC aggregability was present, but low. Endothelial wall stress and NO production may be enhanced for that reason, and feeding of RBC into smaller arterioles at the bifurcations may be more effective by the Fahraeus effect. For the efficiency of the blood O_2 storage during the dive, the micro-vascular HCT in the muscles is important. Hemorheological parameters may be effective on that level, since they can modify this value. For instance, RBC aggregability modulated the intramyocardial HCT gradient in guinea pigs [30].

What might happen during submersion from the hemorheological point of view? It is known that metering from hepatic sinuses or splenic contraction increase the HCT [31,32] and by that way the WBV, too. The decrease of cardiac output by the decrease of heart rate [8] diminishes the blood flow velocity, and intravascular shear rates should be reduced if vessel radius is not balanced essentially. This can turn WBV to still higher values. Muscle flow varies between a complete and a more reduced cutout, depending on the motive of breath hold [33] to result in areas with sufficient flow together with areas of low to zero flow [34]. Specifically, blood with a high viscosity (HCT release and reduction of blood flow velocity) may be pumped through a mosaic of more or less restricted vascular geometries. A high WBV is often displayed clinically as “hyper-viscosity syndrome”. Bleeding of mucous membranes, retinopathy, and neuropathy are typical signs of long-term hyper-viscosity that need to be treated by plasmapheresis in man. Why do diving seals not experience such symptoms? If areas with zero flow exist in the body of seals, shear stress is zero as well there, and the stimulus to dilate the vessels should be restrained. In this situation, shear stress might be lower than the yield stress of blood resulting in blood stasis. In other areas, such as brain, heart, and locomotory muscles, shear stress may be increased. To prevent high capillary pressures and the “hyper-viscosity syndrome”, shear stresses in the micro-vascular network must be reduced. This can be accomplished by plasma skimming with the aid of intravascular phase separation and the formation of a CFLW of relevant magnitude. Indeed, RBC aggregation might be physiologically relevant during diving: (1) Hydrostatic pressures raise RBC aggregation [35], and human volunteers were found to have an increased RBC aggregability when diving to a depth of 300 feet of seawater [36]. (2) In a study comparing free-ranging and captive seals, the free-ranging animals had a higher HCT and RBC aggregability than the captive animals [37]. Our suggestions are hypothetical. It is clear that the importance of RBC aggregability during submerge has to be clarified in a further study.

In conclusion, of the three O_2-stores that are utilized during a dive, blood is unique. Unlike the respiratory and the muscular O_2-store, blood is not stationary, but intermediates exchanges between the two other compartments by its continuous movement. Based on the mechanical properties of the blood cells – which is high deformability and low aggregability of RBC in our Cape fur seals –, blood changes its texture by the intravascular shear forces. It has been thoroughly investigated that the self-assembly of RBC modulates arteriolar diameters through the NO bioavailability. During a dive, the peripheral perfusion may be fine-tuned by this mechanism to prevent a “hyper-viscosity syndrome”. However, our data suggest that blood stasis may be facilitated within specific vascular regions. Our next step will encompass the investigation of the suspension stability of blood at very low shear stresses and the kinetic costs for blood flow. This approach will provide information on the behavior of seal blood during stasis and on the energy demand during the dive from the hemorheological point of view. Preliminary data indicate that the suspension stability of blood is improved in *Otaria flavescens* compared to other mammals (please see the Supplementary File, figure A).

Acknowledgements

The authors are indebted to the Bayworld husbandry teams, especially to Robyn Greyling and Steven Warren for upkeep the animals and maintaining their health and training. We would like to thank Dr. Lucy Runall, Robyn Greyling, and Dr. Ross Kobus for the blood collection. We also thank Dr. Roberto Plasenzotti for his technical assistance at the first visit in Bayworld.

Funding

The National Research Foundation of South Africa supported this work, Program: Knowledge and Collaboration, 2008.

References

1. Butler PJ (2004) Metabolic regulation in diving birds and mammals. Respir Physiol Neurobiol 141: 297-315.
2. Thornton SJ, Hochachka PW (2004) Oxygen and the diving seal. Undersea Hyperb Med 31: 81-95.
3. Thurston GB, Henderson NM (2007) Viscoelasticity of human blood. Handbook of Hemorheology and Hemodynamics. IOS Press, Amsterdam (1stedn) Pp. 72-90.
4. Windberger U, Baskurt OK (2007) Comparative hemorheology. Handbook of Hemorheology and Hemodynamics. IOS Press, Amsterdam (1stedn) Pp. 267-285.
5. Elsner R (1969) Cardiovascular adjustments to diving. The biology of Marine Mammals. Academic Press, New York (1stedn) Pp. 117-145.
6. Butler PJ, Jones DR (1997) The physiology of diving birds and mammals. Physiol Rev 77: 837-899.
7. Ponganis PJ, Knower Stockard T, Levenson DH, Berg L, Baranov EA (2006) Cardiac output and muscle blood flow during rest-associated apneas of elephant seals. Comp Biochem Physiol A 144: 105-111.
8. Ponganis PJ, Meir JU, Williams CL (2011) In pursuit of Irving and Scholander: a review of oxygen store management in seals and penguins. J Exp Biol 214: 3325-3339.
9. Castellini MA, Baskurt O, Castellini JM, Meiselman HJ (2010) Blood rheology in marine mammals. Frontiers in Physiology 146: 1-8.
10. Mezger T (2010) Das Rheologie Handbuch. Vincentz Network, Hannover (1stedn).
11. Nemeth N, Furka A, Alexy T, Baskurt OK, Meiselman HJ et al. (2009) Interspecies differences in hematocrit to blood viscosity ratio. Biorheology 46: 155-165.
12. Plasenzotti R, Stoiber B, Posch M, Windberger U (2004) Red blood cell deformability and aggregation behavior in different animal species. Clin Hemorheol Microcirc 31: 105-111.
13. Windberger U, Bartholovitsch A, Plasenzotti R, Korak KJ, Heinze G (2003) Whole blood viscosity, plasma viscosity and erythrocyte aggregation in nine mammalian species: reference values and comparison of data. Exp Physiol 883: 431-440.
14. Castellini M, Elsner R, Baskurt OK, Wenby RB, Meiselman HJ (2006) Blood rheology of Weddell seals and bowhead whales. Biorheology 43: 57-69.
15. Castellini MA, Castellini JM (1993) Estimation of splenic volume and its relationship to long duration apnea in seals. Phys Zool 66: 619-627.
16. Hedrick MS, Duffield DA, Cornell LH (1986) Blood viscosity and optimal haematocrit in a deep-diving mammal, the northern elephant seal (Mirounga angustirostris). Can J Zool 64: 2081-2085.
17. Cokelet GR, Meiselman HJ (2007) Macro- and micro-rheological properties of blood. Handbook of Hemorheology and Hemodynamics. IOS Press, Amsterdam (1st Edn) Pp. 45-71.
18. Popel AS, Johnson PC (2005) Microcirculation and Hemorheology. Annu Rev Fluid Mech 37: 43-69.
19. Galehr J (2008) Bachelor Thesis. FH Technikum Vienna, Biomedical Engineering.
20. Schmeidl K (2010) Hämorheologische Eigenschaften des afrikanischen Ngunirindes und der Vergleich zum österreichischen Fleckvieh. Diploma Thesis, Veterinary University Vienna.
21. Meiselman HJ, Castellini MA, Elsner R (2001) Hemorheological behaviour of seal blood. Clin Hemorheol 12: 657-675.
22. Boyd IL, Bevan RM, Woakes AJ, Butler PJ (1999) Heart rate and behaviour of fur seals: implications for the measurement of field energetics. Am J Physiol 45: H884-H857.
23. Frangos JA, Eskin SG, McIntire LV, Ives CL (1985) Flow effects on prostacyclin production by cultured human endothelial cells. Science 227: 1477-1479.
24. Malek K, Izumo S (1992) Physiological fluid shear stress causes down-regulation of endothelin-1 mRNA in bovine aortic endothelium. Am J Physiol 263: 389-396.
25. Johnson BD, Mather KJ, Wallace JP (2011) Mechanotransduction of shear in the endothelium: Basic studies and clinical implications. Vasc Med 16: 365-377.
26. Yalcin O, Ulker P, Yavuzer U, Meiselman HJ, Baskurt OK (2008) Nitric oxide generation by endothelial cells exposed to shear stress in glass tubes perfused with red blood cell suspensions: role of aggregation. Am J Physiol Heart Circ Physiol 294: 2098-2105.
27. Ong PK, Jain S, Kim S (2012) Spatio-temporal variations in cell-free layer formation near bifurcations of small arteries. Microvasc Res 83: 118-125.
28. Zhang J, Johnson PC, Popel AS (2009) Effects of erythrocyte deformability and aggregation on the cell free layer and apparent viscosity of microscopic blood flows. Microvasc Res 77: 265-272.
29. Ong PK, Kim S (2013) Effect of erythrocyte aggregation on spatiotemporal variations in cell-free layer formation near on arteriolar bifurcation. Microcirc 20: 440-453.
30. Yalcin O, Aydin F, Ulker P, Uyuklu M, Gungor F et al. (2006) Effects of red blood cell aggregation on myocardial haematocrit using two approaches to increase aggregation. Am J Physiol 290: 765-771.
31. Thornton SJ, Spielman DM, Pelc NL, Block WF, Crocker et al. (2001) Effects of forced diving on the spleen and hepatic sinus in northern elephant seal pups. Pro Natl Acad Sci USA 98: 9413-9418.
32. Hurford WE, Hochachka PW, Schneider RC, Guyton GP, Stanek KS et al. (1996) Splenic contraction, catecholamine release, and blood volume redistribution during diving in the Weddell seal. J Appl Physiol 80: 298-306.
33. Ponganis PJ, Kreutzer U, Stockard TK, Lin PC, Sailasuta N, et al. (2008) Blood flow and metabolic regulation in seal muscle during apnea. J Exp Biol 211: 3323-3332.
34. Blix AS, Elsner RW, Kjekhus JK (1983) Cardiac output and its distribution through capillaries and A-V shunts in diving seals. Acta Physiol Scand 118: 109-116.
35. Chen S, Gavish B, Barshtein G, Mahler Y, Yedgar S (1994) Red blood cell aggregability is enhanced by physiological levels of hydrostatic pressure. Biochim Biophys Acta 1192: 247-252.
36. Taylor WF, Chen S, Barshtein G, Hyde DE, Yedgar S (1998) Enhanced aggregability of human red blood cells by diving. Undersea Hyperb Med 25: 167-170.
37. Wickham LL, Costa DP, Elsner R (1990) Blood rheology of captive and free-ranging northern elephant seals and sea otters. Can J Zool 68: 375-380.