ISSN 2304-3415, Russian Open Medical Journal
2022. Volume 11. Issue 3 (September). Article CID e0304
DOI: 10.15275/rusomj.2022.0304

Original article

Effect of adaptation duration to environmental conditions of the north on morphofunctional restructuring of capillary blood flow

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Received 9 April 2021, Revised 11 January 2022, Accepted 1 February 2022

Abstract: *Background* — We studied blood microcirculation and features of capillary morphology in young men with various duration of adaptation to the environmental conditions of Northeast Russia (Magadan Oblast).
Methods — We examined 211 young men 17-21 years of age who were permanent residents of the North. All study subjects were divided among four groups: Caucasian migrants from central Russia (generation 0) and those born and residing in the North, representing generations 1, 2, and 3. We investigated capillary structure and microcirculation in the eponychium of the nail bed, using a computer-based video capillaroscope, Capillaroscan-1.
Results — We detected the diameter reduction in arterial and intermediate capillary segments with simultaneous absence of a similar pattern in the venous capillary segment along the gradient of generation 0 towards generation 3. We also observed a shorter mean capillary length against the background of a thicker capillary network.
Conclusion — With a longer adaptation period to the environmental conditions of Northeast Russia, compensatory adaptive mechanisms in the capillary network structure and microcirculation are formed, aimed at optimizing capillary blood flow.

Keywords: microhemocirculation, capillaries, young men, adaptation, North.

Cite as Averyanova IV, Vdovenko SI. Effect of adaptation duration to environmental conditions of the north on morphofunctional restructuring of capillary blood flow. *Russian Open Medical Journal* 2022; 11: e0304.

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Introduction

Capillaroscopy is a research method that allows direct in vivo imaging of the skin microcirculation [1]. It is the most practical technique for instantaneous visualization of the skin capillary circulation, aiming at assessing blood flow rate, along with capillary morphological structure and density [2]. Besides, this is an informative procedure for evaluating microvascular changes in the peripheral circulation [3]. Microvasculature constitutes a network of perfused capillaries. It is characterized by minimal heterogeneity in the same person, and is responsible for optimizing microcirculatory perfusion [4], which is autonomously regulated by the metabolic demands of tissues, local angioregulatory mediators, postcapillary oxygen partial pressure (venular-arteriolar communication), and release of vasoactive substances by erythrocytes [5].

It is known that the capillaroscopic picture in different people is characterized by high diversity [6], which often leads to confusion in distinguishing between a normal and pathological picture [7]. The confusion is also explained by the existence of both interindividual and intraindividual variability of the kind in healthy people [8].

The cardiovascular system is a complex transport system, the main function of which is to supply oxygen to metabolizing tissues. Microcirculation is aimed at ensuring oxygen delivery in accordance with the metabolic needs of the entire body, while perfusion pressure is a key element of the microcirculatory system [9].

The functional properties of microcirculation are critically dependent on its angioarchitecture (i.e., the location and morphology of the vessels). Microcirculation undergoes continuous dynamic structural adaptation (remodeling) controlled by hemodynamic and metabolic stimuli [10]. Due to the complexity of interactions between stimuli, responses, and functional properties, an adequate understanding of structural adaptation requires further investigation directly on healthy individuals, with an understanding of morphofunctional restructuring in various environmental conditions. By far, there were just a few studies of microcirculatory parameters in healthy people, and even fewer on the morphofunctional state remodeling of the capillary bed and the microcirculatory parameters in Caucasian individuals with residency of a various duration in the environmental conditions of circumpolar regions.

With a high degree of confidence, we can say that the microcirculatory system is the very first link, which primarily affects adaptive changes in the entire cardiovascular system due to the impact of environmental cold. Those are manifested in changes that help maintaining an adequate level of transcapillary metabolism and optimal tissue nutrition via microcirculation in environmental conditions of the North. In the process of ontogenesis of a particular individual native to the North, it is

reasonable to expect certain manifestations of the phenotypic plasticity, which is not yet fixed at the genotype level but allows optimizing the morphological structure of microvessels in order to maintain homeostasis in severe environmental conditions.

With this reasoning in mind, the objective of our study was to identify the characteristics of blood microcirculation and capillary morphology in young male residents of Magadan Oblast (Northeast Russia) with various residency duration in extreme climatic conditions of the Northeast Russia.

Material and Methods

As a result of a random sampling, we examined 211 young males aged 17-21 years old, permanently residing in Magadan Oblast. Depending on the duration of stay in the region, all examined subjects were distributed among four groups. Group 1 included Caucasian migrants from the central regions of the country, characterized by a short residency in the North (on average, 7.1±1.3 years); we designated this group as *generation 0* (n=38). Group 2 comprised young males who were natives of the region and were born to original migrants; we designated this group as *generation 1* (n=73). Group 3 consisted of young men who were natives in the second generation (n=68), whose parents belonged to generation 1. Group 4 encompassed subjects with the longest period of family residency in the Russian Northeast: these were young men of the third generation, whose parents belong to generation 2 (n=32). The survey participants had no frostbite, hand injuries, or vascular pathologies that could affect microcirculation. Another inclusion criterion for the study was permission to engage in physical education courses as part of an educational program, admission to which students typically receive after passing physical examination by a doctor.

We studied the capillary structure and microcirculation in the nail bed eponychium since this area is easily accessible for examination, and the main axis of capillaries here is parallel to the skin surface whereas in other areas it is visualized as perpendicular [11, 12]. The study was carried out using a drop of immersion oil to maximize the transparency of the keratin layer on the ring finger and little finger of the left hand due to the high light transmission of the skin in these areas [13]. A computer-based video capillaroscope, *Capillaroscan-1* (New Energy Technology LLC, Skolkovo), equipped with an optical probe, was employed in our study. All recordings were made with subjects in a sitting position, at comfortable ambient temperatures of 22-25 °C, in the mornings, after at least a 15-minute rest, with a hand placed at heart level [13].

Capillary network density was assessed in the mode of constructing a panoramic static image of the first line capillary network with an optical magnification of 200x. Presence of characteristic (contrasting) capillaries throughout the entire field of view was a prerequisite. A more detailed analysis was carried out using a 10-second video recording with an optical magnification of 400x of a specific area of the skin, followed by automatic counting of observed capillaries. The device software allowed evaluating all visually observed processes and anatomical structures, along with obtaining mean values for morphometric parameters and red blood cell velocity along the studied capillaries [13].

In the paper, we analyze the following morphofunctional parameters of the microvasculature: the diameter of arterial, venous and intermediate capillary segments (μm), which refers to the area of the vessel lumen filled with visible erythrocytes (since the walls of the vessels per se are virtually indistinguishable under light microscopy); capillary length (μm); the density of the capillary network (arbitrary units), indicating the number of observed capillary loops of the first order (located in close proximity and in contact with the perivascular zone); the size of the perivascular zone (μm), specifically its linear size from the remotest point of this zone to the nearest point of the capillary intermediate segment; blood flow rate in the arterial, venous and intermediate capillary segments (μm/s), reflecting the speed of red blood cell movement in the capillary; deformation coefficient (arbitrary units), reflecting the number of strongly twisted and damaged capillaries; and temperature in the study area, obtained using an infrared radiation receiver of the device (ºC) [14].

Research work was carried out in the period from 2015 through 2017. The study was approved by the Ethics Committee for Medical and Biological Research at the Scientific Research Center, Far Eastern Branch of the Russian Academy of Sciences (protocol No. 3 of December 4, 2012). Written informed consent was obtained from all participants prior to their inclusion in the study.

The obtained material was processed using Statistica 7.0 software package. The normality of the measured variables was checked via Shapiro-Wilk test. All quantitative variables were normally distributed. Results are presented as mean value (M), standard deviation (SD), and standard error (±m). Multivariate analysis of variance (MANOVA) was conducted, followed by a posteriori analysis using the Scheffé test for multiple comparisons. The critical significance level in the study was assumed at p=0.05; 0.01; 0.001.

Results

The structure of capillaries and characteristics of microcirculation in young male residents of the North with various duration of adaptation are presented in the *Table* 1. The results of our study demonstrate that in the process of adaptation to the conditions of the North, a pronounced remodeling of the capillary bed morphofunctional state and of microcirculation characteristics occur. With longer residency in the North (i.e., along the gradient: generations 0, 2 and 3), we observed a smaller diameter of arterial (by 7%) and intermediate (by 5%) capillary segments, with no significant dynamics in the venous segment. Along the same gradient, we have also discovered a significant reduction in the average capillary length (by 6%) against the background of a thicker density of the capillary network (by 5%). Blood flow rates in venous capillary segment tended to diminish by 26%, with the slowest values demonstrated by the examinees of generation 2. The latter also had low blood flow rates in arterial segment, while young male subjects of generation 3 exhibited 16% increase in this parameter. Contrary to the examinees from other groups, young men with the shortest residency in the North (generation 0) yielded higher values in intermediate capillary segments. A significant growth in the values of both deformation coefficient and temperature was observed in the study area along the gradient of generations, 0 to 3.

Table 1. Microhemocirculation in young men of generations 0, 1, 2, and 3

Parameters	*Examined groups*				*Statistical significance of intergroup comparisons*					
	Generation 0 (Group 1)	*Generation 1* (Group 2)	*Generation 2* (Group 3)	*Generation 3* (Group 4)	1-2	2-3	3-4	1-3	2-4	1-4
Arterial segment diameter, µm	8.8±0.62 (0.1)	8.4±0.85 (0.1)	8.5±0.82 (0.1)	8.2±0.57 (0.1)	p=0.007	p=0.477	p=0.049	p=0.048	p=0.130	p=0.001
Venous segment diameter, µm	12.3±1.23 (0.2)	12.1±1.71 (0.2)	12.1±1.65 (0.2)	12.0±1.13 (0.2)	p=0.482	p=0.958	p=0.726	p=0.478	p=0.733	p=0.291
Intermediate segment diameter, µm	17.6±1.82 (0.3)	16.5±1.71 (0.2)	16.3±1.65 (0.2)	16.8±1.13 (0.2)	p=0.009	p=0.467	p=0.082	p=0.008	p=0.293	p=0.004
Capillary length, µm	325.7±34.5 (5.6)	310±45.3 (5.3)	310.6±33 (4.0)	306.4±27.7 (4.9)	p=0.035	p=0.591	p=0.255	p=0.083	p=0.618	p=0.003
Capillary network density, arb. units	0.0391±0.004 (0.0006)	0.0407±0.004 (0.0005)	0.0408±0.004 (0.0005)	0.0410±0.003 (0.0005)	p=0.045	p=0.963	p=0.749	p=0.025	p=0.719	p=0.011
Perivascular zone size, µm	90.7±8.01 (1.3)	90.9±12 (1.4)	91.9±11.6 (1.4)	92.6±6.22 (1.1)	p=0.921	p=0.614	p=0.338	p=0.527	p=0.137	p=0.091
Arterial segment blood flow rate, µm/s	225.8±56.1 (9.1)	200.1±55.5 (6.5)	193.9±51.1 (6.2)	230.3±53.7 (9.5)	p=0.049	p=0.451	p=0.005	p=0.006	p=0.006	p=0.747
Venous segment blood flow rate, µm/s	182.1±37.6 (6.1)	142.8±41.9 (4.9)	133.6±43.7 (5.3)	153±35.6 (6.3)	p=0.001	p=0.185	p=0.008	p=0.001	p=0.181	p=0.008
Intermediate segment blood flow rate, µm/s	218.0±41.3 (6.7)	159.6±59 (6.9)	173.3±44.5 (5.4)	183.1±35.1 (6.2)	p=0.001	p=0.121	p=0.288	p=0.001	p=0.009	p=0.001
Deformation coefficient, arb. units	0.29±0.06 (0.01)	0.31±0.09 (0.01)	0.32±0.08 (0.01)	0.35±0.06 (0.01)	p=0.155	p=0.484	p=0.002	p=0.003	p=0.001	p=0.001
Temperature, °C	30.51±1.54 (0.25)	31.01±1.79 (0.21)	31.02±1.73 (0.21)	31.55±1.36 (0.24)	p=0.133	p=0.968	p=0.100	p=0.121	p=0.094	p=0.009

The results are presented as mean (M), standard deviation (±SD), and standard error (m).

Discussion

Based on the assumption that changes in parameter values reflecting the morphological and functional characteristics of the microvasculature are adaptive, it can be assumed that an increase or reduction of the diameter, as well as blood flow rates in arterial, venous, or intermediate capillaries, would contribute to the optimization of local heat production and tissue nutrition via microcirculation.

The analysis of capillaroscopic patterns in young male subjects representing generations 0, 1, 2, and 3 revealed a number of essential features in the structure of the capillary network that are formed in the process of adaptation to the conditions of the North. Each capillary loop is represented by a thinner arterial segment, and wider venous and intermediate segments (or capillary apex) [15]. The venous segment is the efferent link of the capillary loop, and the arterial segment is its afferent link. The diameters of the afferent and efferent links at the widest point are the diameters of the arterial and venous segments, respectively [15]. It is known that the capillary diameter is the structural parameter that largely determines the volume of blood flow passing through the microvasculature throughout its entire length [16]. The obtained results implied a significant reduction in the diameter of arterial capillaries with the duration of adaptation to the environmental conditions of the North. It should be noted that the norm for the arterial segment diameter ranges from 7 to 17 µm (on average, 11.91±1.87 µm) [15]. Comparing our results with the reference range, we concluded that subjects with the longest duration of adaptation to the conditions of the North had capillary diameter closely approaching its lower limit. A similar trend was observed with respect to the venous capillary diameter, with the reference range of 11-20.6 µm (on average, 15±2.42 µm) [15]. A capillary constriction with a diameter approaching the lower limit of the reference range was also found, although we could hardly see any change in the parameter throughout the sample, from generation 0 to generation 3. According to some authors, the ratio of venous diameter to arterial diameter is approximately 1.2-1.5:1 [8], which is entirely consistent with our results.

Our findings indicate that in the process of a long-term exposure to the extreme conditions of the North, the region-specific features are formed in the structure of the microvasculature, which is manifested by a lumen size reduction of the arterial and intermediate segments of the capillary network. We propose that such pattern is associated with a prolonged cold-induced vasoconstriction caused by an increasing inability of smooth muscle cells in the vessel to relax until the temperature threshold is reached [17]. Reflex vasoconstriction, mediated by sympathetic influence in response to the need for avoiding heat loss, occurs after the binding of noradrenaline to α1 and α2 adrenoreceptors on the vascular smooth muscle cell membrane [18].

As for the venous segment of microcirculation, despite the absence of significant intergroup changes in diameter, a decrease in the blood flow rate in the venous capillary segment in consecutive generations is clearly recorded. It is known that one of the main conditions for adequate transcapillary exchange is the time of direct contact of substances with the vascular wall, which, in turn, depends on the capillary size (exchange surface area) and blood flow rate [14]. Faster blood flow naturally reduces the contact time and, accordingly, deteriorates an efficacy of transcapillary exchange. Based on this, the adaptive nature of such changes becomes obvious, when the processes of reducing the lumen of the arterial and intermediate segments with a simultaneous increase in the arterial segment blood flow rate are observed against the background of no changes in the diameter of the venous capillary segment and a consistent reduction in the blood flow velocity in these capillary areas, which contributes to the optimal tissue nutrition via microcirculation in environmental conditions of the North.

The capillary loop diameter in its intermediate segment normally ranges 8 to 21 µm (17.17±2.12 µm on average) [15]. An analysis of this parameter revealed that with an increase in the duration of residency in the conditions of the North, a decrease in the diameter of the intermediate capillary segment was observed. At the same time, in contrast to the values of the arterial and venous segments, the average values of which were at the lower limit of the norm, those of intermediate segment were within the reference range. We assume that such balance in maintaining proper diameter in each capillary segment aims at improving transcapillary exchange, which largely meets the metabolic needs of the body in the conditions of the North [4].

The number of capillaries per unit area of the skin simultaneously involved in blood flow is called the density of the capillary network [19], which characterizes the intensity of transcapillary exchange [16]. The nature of changes observed in our study implies an increase in the density of the capillary network along the gradient from generation 0 to generation 3. This finding could be considered evidence of a tendency to

optimize the perfusion capacity of the microcirculatory bed in response to augmented metabolic needs of the body [14] with a longer duration of adaptation to the North.

We analyzed gas and metabolite exchanges occurring in the intermediate capillary segment. They seemed to match the reference range, along with a thicker capillary density. Both findings allowed assuming that they were aimed at meeting the needs of cardiovascular system in gas exchange and metabolic functions, which supported our earlier results concerning an optimization of gas exchange function with a longer adaptation period to the northern extreme conditions. The latter is manifested by higher oxygen utilization factor, a more efficient rate of oxygen consumption and carbon dioxide excretion per each instance of breathing, against the background of a reduction in basal metabolism [20].

We also analyzed capillary length, which exhibited similar pattern of becoming smaller with duration of adaptation to the North. We compared the obtained results with the reference range suggested by foreign authors, 92-295 µm (on average, 240±38.3) [13], and found that in all examined groups of subjects, capillary length values exceeded its upper limit, with the longest capillaries observed in young men with the shortest duration of adaptation to the North. We believe that longer capillaries habitually indicate arterial hypertension [21]. Despite the conclusion that microcirculatory system of self-regulating capillaries is independent of systemic arterial pressure [9], which was confirmed in our previous study, subjects with the shortest period of adaptation exhibited stress in cardiovascular system functioning, manifested by an increase in systolic blood pressure, total peripheral vascular resistance, and heart rate; with a simultaneous reduction in the stroke volume of the blood. All listed parameters optimized in generation 3 subjects with the longest adaptation to the environmental conditions of the North.

Perivascular zone size reflects the degree of hydration in the interstitial space and is normally under 100 µm [23]. Our results revealed no significant differences among the groups, which also indicated that the obtained values corresponded to the norm for this parameter.

Skin microcirculation, in addition to the above functions, is responsible for thermoregulatory metabolism [24]. Increased skin temperature in the study area in young men with a longer period of adaptation to the North implied intensified blood flow in their bodies [25].

Capillary deformation coefficient was within its physiological norm in all four groups; however, its significant growth was detected along the gradient of generation 0 to generation 3, caused apparently by chronic exposure to cold.

We established statistically significant differences in morphological structure and functional indicators of microhemocirculation between the groups along the gradient of generation 0 to generation 3: a smaller diameter of arterial segment, the optimum size of intermediate segment, a thicker density of capillary network, a shorter length of capillaries, as well as a lower rate of arterial blood flow were exhibited by young male subjects of generation 3, compared with those of generations 1 and 2. In addition, lower blood flow rate in venous and intermediate capillary segments was typical for the subjects of generation 1, as compared to migrants (generation 0), with these indicators taking higher values with a duration of the adaptation period to environmental conditions of the North. The reduction in the diameter and length of the arterial segment observed in individuals with a longer adaptation to the North (generation 3) was much lower than the results presented by other authors [26]. It should be noted that an overall increased density of the capillary network and high blood flow rate in arterial capillary segments, apparently, ensures the optimization of blood flow, as evidenced by a higher temperature in the studied area of the hand.

Discovered adaptive mechanisms of microhemocirculation are optimal for maintaining body temperature homeostasis, the best level of cardiovascular system functioning, gas exchange function, and overall oxygen supply, which is fully consistent with the data obtained in our previous research.

Conclusion

The results of our study implied that architectural rearrangements of microvascular beds depended on the duration of adaptation to the environmental conditions of the North. Such compensatory adaptive regional features were manifested by a smaller diameter of the arterial segment of capillaries against the background of maintaining optimal dimensions of their intermediate segment with a simultaneous increase of their average length.

Study limitations

The limitation our study was associated with a narrow age range of our subjects (17–21 years old); hence, our sample exclusively represented young age.

Ethical considerations

Various ethical issues (plagiarism, informed consent, misconduct, data fabrication and/or falsification, duplicate publications and simultaneous submissions, redundancy, etc.) were observed by the authors.

Conflict of interest

The authors declare no conflicts of interest.

Funding

The study was supported by the budget financing of the ARKTIKA Scientific Research Center, Far Eastern Branch of the Russian Academy of Sciences, Magadan, Russia

Ethical approval

All procedures performed in pour study, involving human participants, complied with the ethical standards of the institutional and national research committee and with 1964 Declaration of Helsinki and its later amendments, or comparable ethical standards.

References

1. Ocampo-Garza SS, Villarreal-Alarcón MA, Villarreal-Treviño AV, Ocampo-Candiani J. Capillaroscopy: A valuable diagnostic tool. *Actas Dermosifiliogr (Engl Ed)* 2019; 110(5): 347-352. https://doi.org/10.1016/j.adengl.2019.04.009.
2. Hosking SP, Bhatia R, Crock PA, Wright I, Squance ML, Reeves G. Non-invasive detection of microvascular changes in a paediatric and adolescent population with type 1 diabetes: A pilot cross-sectional study. *BMC Endocr Disord* 2013; 13: 41. https://doi.org/10.1186/1472-6823-13-41.
3. Emrani Z, Karbalaie A, Fatemi A, Etehadtavakol M, Erlandsson BE. Capillary density: An important parameter in nailfold capillaroscopyм.

Microvasc Res 2017; 109: 7-18. https://doi.org/10.1016/j.mvr.2016.09.001.

4. De Backer D, Durand A. Monitoring the microcirculation in critically ill patients. *Best Pract Res Clin Anaesthesiol* 2014; 28(4): 441-451. http://doi.org/10.1016/j.bpa.2014.09.005.
5. Segal S. Regulation of blood flow in the microcirculation. *Microcirculation* 2005; 12(1): 33-45. https://doi.org/10.1080/10739680590895028.
6. Andrade LE, Gabriel Júnior A, Assad RL, Ferrari AJ, Atra E. Panoramic nailfold capillaroscopy: a new reading method and normal range. *Semin Arthritis Rheum* 1990; 20(1): 21-31. https://doi.org/10.1016/0049-0172(90)90091-s.
7. Gutierrez M, Bertolazzi C, Tardella M, Becciolini A, DI Carlo M, Dottori M, et al. Interreader reliability in assessment of nailfold capillary abnormalities by beginners: Pilot study of an intensive videocapillaroscopy training program. *J Rheumatol* 2012; 39(6): 1248-1255. https://doi.org/10.3899/jrheum.111299.
8. Bollinger A, Fagrell B. Clinical capillaroscopy: A guide to its use in clinical research and practice. Toronto: Hogrete & Huber Publishers. 1990; ix, 166 p. https://www.worldcat.org/title/22182568.
9. Moore JP, Dyson A, Singer M, Fraser J. Microcirculatory dysfunction and resuscitation: Why, when, and how. *Br J Anaesth* 2015; 115(3): 366-375. https://doi.org/10.1093/bja/aev163.
10. Pries AR, Secomb TW. Modeling structural adaptation of microcirculation. *Microcirculation* 2008; 15(8): 753-764. https://doi.org/10.1080/10739680802229076.
11. Cutolo M, Grassi W, Matucci Cerinic M. Raynaud's phenomenon and the role of capillaroscopy. *Arthritis Rheum* 2003; 48(11): 3023-3030. https://doi.org/10.1002/art.11310.
12. Grassi W, Del Medico P. Atlas of Capillaroscopy. Milan: Edra Medical Publishing and New Media. 2004; 302p. Italian. https://www.worldcat.org/title/804166730.
13. Lambova SN. The Role of Capillaroscopy in Rheumatology. PhD thesis. Giessen. 2011; 192 p. German. https://core.ac.uk/download/pdf/56350441.pdf.
14. Fedorovich AA. The capillary hemodynamics in eponychium of upper extrmity. *Regional Blood Circulation and Microcirculation* 2006; 5(1): 20-29. Russian. https://www.elibrary.ru/item.asp?id=11715560.
15. Etehad Tavakol M, Fatemi A, Karbalaie A, Emrani Z, Erlandsson BE. Nailfold capillaroscopy in rheumatic diseases: Which parameters should be evaluated? *Biomed Res Int* 2015; 2015: 974530. https://doi.org/10.1155/2015/974530.
16. Kozlov VI. Histophysiology of the microcirculation system. Regional Blood Circulation and Microcirculation 2003; 2(3): 79-85. Russian. https://www.elibrary.ru/item.asp?id=13074553.
17. Bergersen TK, Eriksen M, Walløe L. Local constriction of arteriovenous anastomoses in the cooled finger. *Am J Physiol* 1997; 273(3 Pt 2): R880-R886. https://doi.org/10.1152/ajpregu.1997.273.3.R880.
18. Witzleb E. Functions of the Vascular System. In: Schmidt RF, Thews G, Eds. Human Physiology. Heidelberg, Berlin: Springer. 1989: 480-542. https://doi.org/10.1007/978-3-642-73831-9_20.
19. Alivernini S, De Santis M, Tolusso B, Mannocci A, Bosello SL, Peluso G, et al. Skin ulcers in systemic sclerosis: Determinants of presence and predictive factors of healing. *J Am Acad Dermatol* 2009; 60(3): 426-435. https://doi.org/10.1016/j.jaad.2008.11.025.
20. Averyanova IV, Vdovenko SI, Maksimov AL. Evaluation of the impact of environmental conditions on the status of the body of young people of 17-19 years of different ethnic groups of the North-east Russia. Hygiene and Sanitation 2017; 96(8): 766-769. Russian. http://doi.org/10.18821/0016-9900-2017-96-8-766-769.
21. Lo LC, Lin KC, Hsu YN, Chen TP, Chiang JY, Chen YF, et al. Pseudo three-dimensional vision-based nail-fold morphological and hemodynamic analysis. *Comput Biol Med* 2012; 42(9): 873-884. https://doi.org/10.1016/j.compbiomed.2012.06.001.
22. Averyanova IV, Vdovenko SI. Indicators of the cardiovascular system in the caucasian residents of Magadan Region depending on the term of residing under conditions of Russia'' Northeast. *Yakut Medical Journal* 2018; (4): 89-91. Russian. https://doi.org/10.25789/YMJ.2018.64.27.
23. Fedorovich AA. Non-invasive evaluation of vasomotor and metabolic functions of microvascular endothelium in human skin. *Microvasc Res* 2012; 84(1): 86-93. http://doi.org/10.1016/j.mvr.2012.03.011.
24. Camargo CP, Gemperli R. Endothelial function in skin microcirculation. In: Da Luz PL, Libby P, Chagas ACP, Laurindo FRM, Eds. Endothelium and Cardiovascular Diseases. Vascular Biology and Clinical Syndromes. Academic Press. 2018; 673-679. https://doi.org/10.1016/b978-0-12-812348-5.00047-7.
25. Johnson JM, Kellogg DL Jr. Thermoregulatory and thermal control in the human cutaneous circulation. *Front Biosci (Schol Ed)* 2010; 2(3): 825-853. https://doi.org/10.2741/s105.
26. Lambova S, Müller-Ladner U. Nailfold capillaroscopy of the toes in healthy subjects. *Annals of the Rheumatic Diseases* 2015; 74(2): 1262-1264. http://doi.org/10.1136/annrheumdis-2015-eular.5709.

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