

**CONGRESS SESSIONS**  
*Aging*

# Role of Oxidative Stress in Mechanisms of Premature Aging in Shift Labor Workers

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## Abstract

There have been examined 90 practically healthy male-shift-workers 21-58 aged and 21-60 aged (average age  $41.4 \pm 1.4$  and  $48.6 \pm 1.3$ ) who worked for a long period of time in the North on shift at the enterprises of JS "Yamburggasdobycha" at the moment of examination. It was revealed a high content of glycosaminoglycans (GAG) in blood serum ( $2.20 \pm 0.12$  mmol/l), accumulation of LPO products ( $3.45 \pm 0.18$  nmol MDA/ml) against the background of decreased glutathione reductase activity ( $0.38 \pm 0.04$  mkmol/l hour). Level of total cholesterol was increased at standard content of HDL ( $6.1 \pm 0.2$ ). It can be concluded that definition of GAG and MDA in blood is one of the significant criteria, reflecting adaptive tension and premature aging of shift-workers.

*Key words:* glycoaminoglycans, premature aging, shift work, oxidative stress

## INTRODUCTION

Oxidative stress is of great importance in pathogenesis of such diseases as atherosclerosis, diabetes mellitus, ischemic heart disease, and cancerogenesis. Active oxygen forms (AOF) affecting biologically significant molecules (lipids, proteins, nucleonic acids) are the main "tool" of oxidative stress. High reactogenic properties of active oxygen forms are explained by their unstable molecules. However, oxidative stress possesses not only cytotoxic properties but plays a great role in adaptation, intercellular relations and intracellular reactions because oxygen forms can be the secondary messengers maintaining the physical-chemical properties of biological membranes, cellular redox systems, protein kinase activity, regulating such cellular reactions as proliferation, differentiation and apoptosis. Oxidative stress is considered to be imbalance between presence of oxidants and anti-oxidants in a biological system towards oxidants prevalence, accompanying anti-oxidants depression, presenting special enzyme systems, water- and fat soluble anti-oxidants. It should be noted that in different organs and tissues active oxygen metabolites as well as anti-oxidant content by enzyme and non-enzyme nature are significantly different. Naturally, in tissues with active oxygen metabolism both an increased generation of active oxygen metabolites and anti-oxygen and anti-radical systems activity are observed there, including fat-soluble antioxidant content. Balance between the system of generation and AOF utilization, forming at oxidative stress,

can form at different stages of imbalance. In recent years there are a lot of scientific works proving a great role of oxidative stress in pathogenesis of aging. This role is connected with participation of both AOF and anti-oxidants in metabolism of extracellular matrix (ECM) of connective tissue. Oxidative stress plays an important role in accelerating the aging in the extreme conditions, namely, in the Far North. Human state of specific ecological tension in the Far North was called by us "Syndrome of polar tension". This syndrome isn't considered to be a pathological state. It characterizes the features of adaptive process and their trends in influence of the ecological northern factors on a human. The complex of electromagnetic phenomena connected with the solar activity is the main factor forming the Syndrome. It is more expressed along the 67<sup>th</sup> parallel called an auroral zone. Namely in this zone the northern lights are manifested in the most degree. So here we can see the greatest range of geomagnetic field oscillations. It is known that aging is based on some changes of metabolism in connective tissue, so in our work we estimated blood glycosaminoglycans content (GAG) as the indices reflecting intensity of metabolism in connective tissue as well as lipid peroxidation products and some anti-oxidative systems.

## MATERIAL AND STUDY DESIGN

We have examined 90 practically healthy male-shift-workers aged 21-58 and 21-60 (average age  $41.4 \pm 1.4$  and  $48.6 \pm 1.3$ ) who worked for a long period of time in the North on shift at enterprises of IS "Yamburggasdobycha" at the moment of examination. LPO products based on the level of final LPO products (MDA) in blood serum<sup>[1]</sup>, sulphhydryl group content (SH-groups,<sup>[2]</sup>) glutathione reductase activity (GR,<sup>[3]</sup>), ceruloplasmin content (TsP<sup>[4]</sup>), glycosaminoglycans<sup>[5]</sup> have been estimated. Besides, cholesterol content, LDL have been determined, enzyme activity (alkaline phosphatase (Aph), gamma-glutamyltransferase (GGT) and amylase have been estimated by the known methods.

## RESULTS

In general it was revealed a high GAG content in blood serum ( $2.20 \pm 0.12$  mmol/l), accumulation of LPO products ( $3.45 \pm 0.18$  nmol MDA/ml) on the background of decreased glutathione reductase activity ( $0.38 \pm 0.04$  mkmol/hour). At LDL

content in norm the level of total cholesterol was significantly higher.

To prove the most information indices showing some features of shift labor in the North as well as the criteria of beginning fatigue from this kind of work, the structure of interrelation between the indices studied was estimated, using the methods of regressive analyses. The data are shown in Figure 1.

Fig. 1 presents dependence between GAG contents in blood and the northern period of living, in this case a stable regularity showing that at increase of the northern period GAG contents in blood increase. It reflects enhancing destruction in connective tissue that can be interpreted as acceleration of organism aging processes yet.

As we see at Fig.2, the regularities between GAG contents in blood and duration of shift labor has a negative character compared to correlation with the northern period of living. So we consider that it is not only disorders of metabolism activity but there are deep structural changes in the connective tissue in shift workers, which increase in dependence on duration of work. Taking into consideration the fact that lipid peroxidation is of a great importance in change of metabolism velocity in connective tissue as well as acceleration of aging, further, we have studied the nature of interrelation between the indices studied and MDA content in blood. MDA (malovic dialdehyde) concentration in blood generally reflects peroxidation activity.

Interrelation between MDA content in blood and duration of work on shift has been analyzed. Fig.3 presents these data. As we can see, this regularity has a phase character. First at increased duration of work on shift, MDA content in blood as well as activity of peroxidation decreased. As it follows from our early work, this regularity reflects the tension of organism regulatory and homeostatic systems. Two types of reactions have been revealed. An increased duration of working results in a decreased peroxidation activity or it remains without changes (1<sup>st</sup> type). Positive correlation between peroxidation activity and increased tissue destruction as well s duration of shift labor are typical for 2<sup>nd</sup> type of reaction. Thus, definition of MDA in blood of shift labor workers, reflecting the intensity of the northern oxidative stress can be considered an important prognostic criterion showing the increase of connective tissue destruction followed by development of disadaptive (prepathological) states.

Hypothetic scheme, reflecting interrelation between content of connective tissue metabolism products (GAG) in blood, content of lipid peroxidation products and SH- groups level.

## CONCLUSION

Thus, based on the conducted analyses, we can offer the following variants of interaction between the systems of connective tissue and LPO in dependence on duration of action of the extreme factors of working on shift. This variant of reaction (1-2 periods) accompanied by increasing adaptive tension reflects transition of regulatory and homeostatic systems to a new, more intensive level of function.

The 3<sup>rd</sup> period is characterized by development of the syndrome of hyperoxidation.

Against the background of relative depression of anti-oxidation systems (example SH-groups), sharp decrease of GAG content in blood testifies to the decreased metabolic processes in connective tissue because of increasing of structural, qualitatively new changes. So, determination of GAG, MDA and SH-groups content in blood is the main criteria reflecting state of adaptive tension and process of premature aging in shift labor workers.

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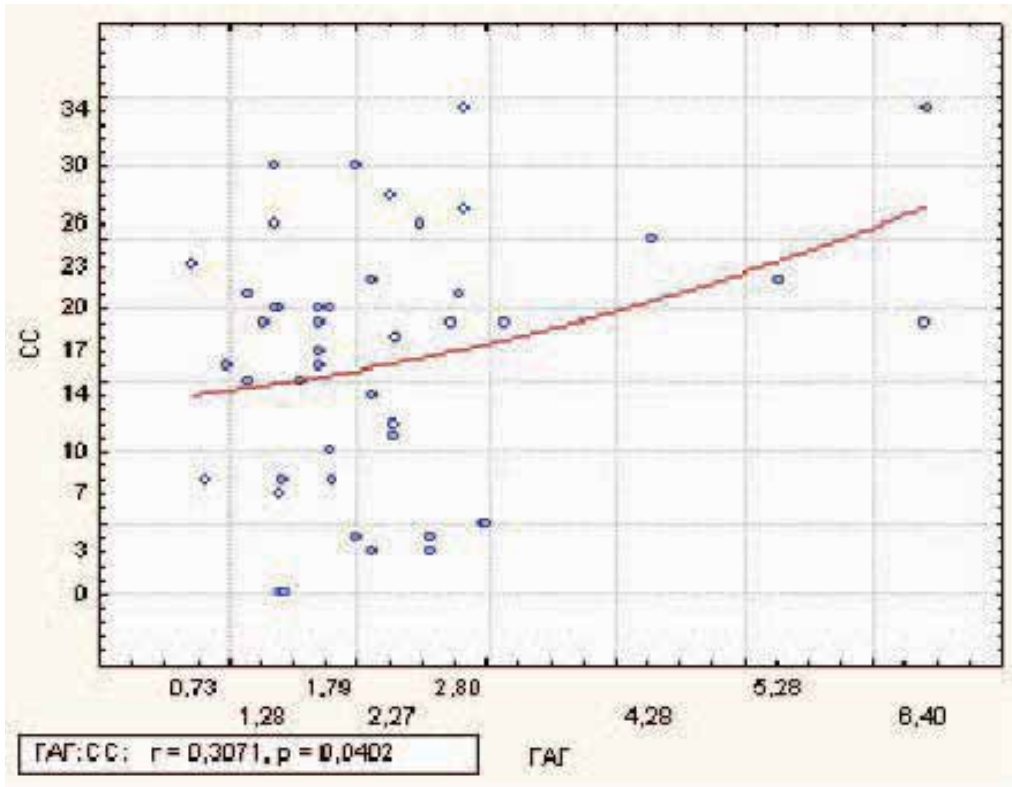


Fig.1 Dependence between GAG contents in blood and the northern period of living (Abscess axis □GAG contents in blood, coordinate axis □the northern period of living ).

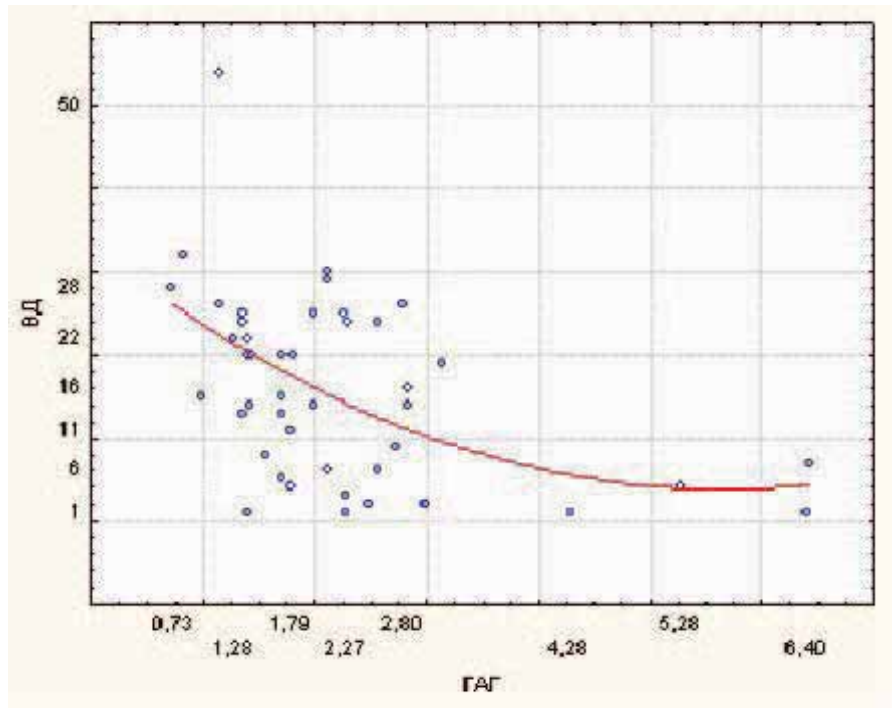


Fig.2 Dependence between GAG contents in blood and duration of shift labor  
 (Abscess axis □GAG contents in blood, coordinate axis □duration of shift labor in years)

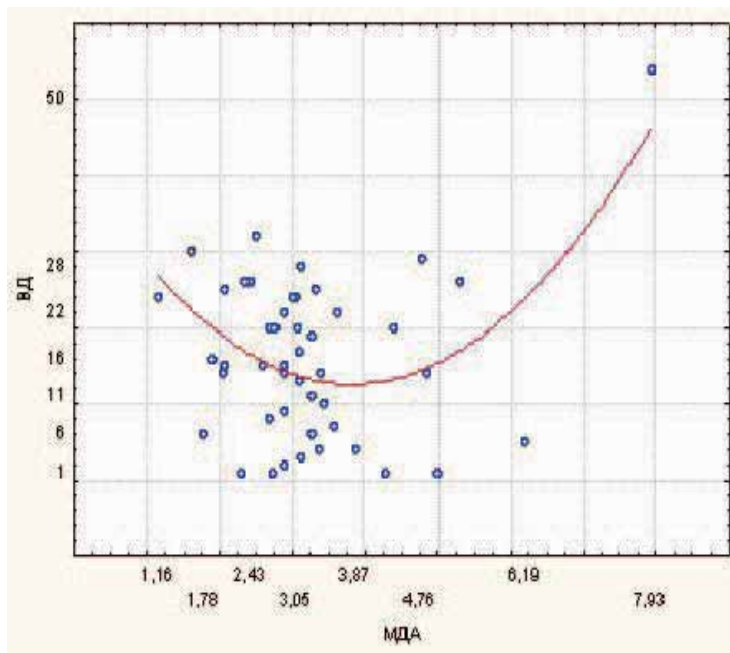


Fig.3. Interrelation between MDA content in blood and duration of shift labor.

# *The Aging Population and Naturally Occurring Retirement Communities (NORCs); Local Government, Healthy Aging, and Healthy-NORCS*

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**Background:** The term Naturally Occurring Retirement Communities (NORCs) has been used since the 1980s. NORCs are defined as communities where people remain or move to when they retire. NORCs develop ‘naturally’, meaning that seniors tend to remain or move there when they retire, although the residences and physical environment were not constructed for a senior population. The term, Healthy-NORC, has been introduced and is associated with healthy aging. **Objectives/Methods:** We describe how demographic trends will facilitate a dramatic growth in NORCs. Acknowledging the ‘Determinants of Health’ model, we suggest that some determinants impact people differently at different ages. We also suggest that more attention be focused on the impact of physical/social environments on health, and that some determinants of health are particularly relevant for seniors. We argue that NORCs exist on a spectrum, from NORC to H-NORC, and that health benefits for seniors increase as NORCs adopt additional characteristics associated with improved senior health. We also illustrate H-NORC research methods and policy options for local governments. **Results/Conclusion:** Compared to the provision of additional medical and social services, H-NORCs represent a low-cost approach to facilitating healthy aging. Municipal governments can promote healthy aging and should pursue policies that will stimulate H-NORC development.  
*Key words: Naturally Occurring Retirement Communities, NORCs, Healthy-NORCs, healthy aging, retired, seniors, municipal government*

## **INTRODUCTION**

Hunt introduced the term Naturally Occurring Retirement Community (NORC) in the 1980s after surveying locations in Madison, Wisconsin (USA), that appeared to have high concentrations of retired people residing in a particular geographic area.<sup>[1,2]</sup> NORCs were described as developing naturally because seniors remained or moved to the locations which were not specifically designed or constructed for a senior population.<sup>[3,2]</sup> The influence of increasing concentrations of seniors resulted in the development of communities with distinct senior friendly characteristics. Masotti et al (2006) suggested that NORCs “exist on a spectrum in which some NORCs progressively illustrate increased ‘senior friendly’ organization in their political, social, and physical environments. They also introduced a new term ‘Healthy – Naturally Occurring Retirement Communities<sup>[4]</sup>, which they described as:

“...a community with environmental characteristics that positively affect senior-sensitive determinants of health. The environmental characteristics act to facilitate increased physical activity, social interaction, and a sense of community and well-being. The mere provision of additional medical or social services to seniors living in a NORC is not sufficient to justify the designation of an H-NORC.”<sup>[5]</sup>

In the previous paper, Masotti et al (2006) primarily focused on North American demographic trends as presenting evidence of the need to address NORCs as a growing phenomenon. They also provided supporting evidence and discussed the concepts of: a) senior-sensitive determinants of health, b) Healthy-NORCs, and c) the possibility that NORCs exist on a NORC to Healthy-NORC spectrum. In this paper we argue that the NORC phenomenon has international relevance given the global trend towards aging populations and urbanization. We will also discuss the concept that NORCs can develop in all communities with different Socio-Economic Status (SES) characteristics and that all NORCs can adopt characteristics making them healthier for seniors. We finish by suggesting that (since all communities can develop NORCs and all NORCs can become healthier) there is a role for all municipal governments in promoting healthy aging by facilitating the growth of Healthy-NORCs.

## **BACKGROUND**

In *Healthy Naturally Occurring Retirement Communities: A Low-Cost Approach to Facilitating Healthy Aging*, Masotti et al argued that the physical and social environments significantly impact the health of populations. They also suggested that, since the retired spend more time in the community, there exists a dose-response relationship between the local environment and health and that this suggested that some NORCs (i.e., Healthy-NORCs) are healthier for seniors than others because of the positive impact of the combined physical and social environments. The main points presented in their paper included the following:

“a) that demographic trends, such as increasing average population age and the desire of today’s seniors to ‘age in place’, will facilitate a dramatic growth in

NORCs; b) that substantial attention be focused on the impact of physical and social environments on health; c) that some determinants of health are more relevant for seniors; d) that there are health benefits of living in NORCs for seniors; e) the amount of health benefits increase as NORCS adopt additional characteristics associated with increased quality of life and better health for seniors; f) it will become increasingly apparent that NORCs exist on a spectrum, from NORC to Healthy-NORC; and g) physical, social and political environmental characteristics will evolve as the population ages and the local government and private sector respond to the increased political and market power of the senior population.”<sup>[5]</sup>

Although NORC literature has generally focused on North America, it is clear that international demographic trends also indicate the potential for NORCs to develop in urban communities throughout the world.

#### **DEMOGRAPHIC TRENDS □ EXPECT NORCS TO BE AN INTERNATIONAL PHENOMENON**

The main factor governing the emergence and growth of NORCs involves an increasing desire to ‘age-in-place’ among the growing elderly population.<sup>[6-9]</sup> NORCs tend to develop in cities because of the increased access to goods, services and social opportunities. Current North American seniors are more prosperous than ones in previous generations.<sup>[10,11]</sup> They are living longer and experiencing lower rates of disability while remaining healthier and more active.<sup>[12]</sup> When a sufficient number healthy seniors reside in a specific area, they will influence the social environment and create a more active and vibrant senior oriented community.

The trend towards urbanization and aging-in-place is not only a North American phenomenon. It has been recognized internationally. The United Nations predicts that the percentage of urban dwellers will increase from 47% in 2000 to 60% in 2030.<sup>[13,14]</sup> Much of this increase will be attributed to the aging senior population. For example, in Canada and the United States about 80% of seniors live in cities.<sup>[13-17]</sup> Thus, based upon the global trends of aging populations and urbanization, it is reasonable to assume that a large percentage of seniors worldwide will also prefer to age-in-place. As a result, we can expect NORCs to become an international phenomenon which will demonstrate continued growth in both numbers and proportion of the population.

#### **SOCIO-ECONOMIC-STATUS: NORCS CAN DEVELOP ANYWHERE**

What makes NORCs unusual social phenomena is that they can develop regardless of the particular residents’ SES. Moreover, NORCs can feature a variety of economic and social characteristics that may be homogeneous or heterogeneous relative to the larger surrounding areas in which the NORCs exist. It is important to remember that NORCs can be communities within communities where examples include: a) small geographic areas such as a city block or groups of

blocks, b) apartment complexes; or c) groups of condominiums or single family houses. Generally, a NORC is defined as a community with a high concentration of retired people residing in an area that was not explicitly designed or planned for seniors.<sup>[2,3,18]</sup>

Depending upon the characteristics of the surrounding area, individual NORCs can include wealthy seniors, poor seniors or a blend of both. NORCs can also form across ethnic, religious, and racial demographic lines given that the governing factors in their development do not directly involve wealth, previous occupational status or other SES variables. In other words, NORCs can develop in all communities, because all people who continue to live will age, eventually retire, and must live somewhere. Examples of SES variance can be found in American NORCs include: a) whites residents living along side blacks and Hispanics in Baltimore; b) locations where incomes range from low to high such as in Cleveland; and c) where religious diversity exists, via tenancies of Jews, Protestants, and Catholics in Philadelphia or a largely Jewish immigrant composition such as in Pittsburgh.<sup>[19]</sup>

As communities experience demographic shifts such as an increasingly older population, the community will also experience senior influenced change in the number of characteristics by which it can be identified as a NORC. Public amenities that previously have been devoted to a broad demographic setting may increasingly be converted for uses more common to an aging and/or elderly population. Examples that could occur include the conversion of schools, housing, streets, parks, coffee shops, restaurants or pubs into places where seniors meet and become more physically and socially active.<sup>[20]</sup> In an other example, the park gazebo or coffee shop may naturally evolve into major centers of social or physical activities for seniors.

#### **HEALTHY-NORCS AND THE ROLE OF MUNICIPAL GOVERNMENTS**

In *Healthy Naturally Occurring Retirement Communities: A Low Cost Approach to Facilitating Healthy Aging*, Masotti et al (2006) suggested that NORCs exist on a NORC-to-Healthy-NORC Spectrum.<sup>[5]</sup> This was because all NORCs have characteristics that are attractive and accommodating towards seniors who have decided to stay or move there. However, some NORCs are healthier for seniors than others because the Healthy-NORCs have adopted more characteristics of the physical/social environment that are associated with improved health or quality of life for seniors.

The main point made was that: “... *the physical environment may be the most important characteristic that facilitates the evolution from NORC to healthy NORC. It can provide opportunities for developing vibrant social and physical environments that also provide a sense of community □ a clean, safe, secure, and socially welcoming interactive residential area.*”<sup>[5]</sup> If this is true, it is clear that all municipal governments worldwide possess some ability to promote healthy-aging by making even minor changes to the physical environment that promote physical

and social activities and foster a sense of safety and community.

In Table 2, Masotti et al illustrated diverse examples of policy initiatives that may be a fit for a given municipality. In this paper, we suggest that local governments that are interested in promoting healthy aging (via facilitating the development of Healthy-NORCs), could start with a three-step approach. First, identify a variety of community-specific policy options that may move the local NORC along the NORC to Healthy-NORC spectrum. Second, evaluate the political and economic feasibilities of each policy option. And third, begin by implementing the most feasible options. It will be clear that some of the options identified easily fall within the abilities of most local governments. One simple example is to add and/or maintain street lights so that seniors residents feel more comfortable walking after dark. In the right neighborhood, this decision could dramatically increase the amount of physical and social activities of seniors. It may even have a positive impact on local businesses.

## CONCLUSION

NORC awareness by both government and private sectors has increased in North America. For example, policy designed to accommodate present and future NORC environments is being studied at the municipal level in American jurisdictions such as Syracuse/Onondaga county in upstate New York.<sup>[21,22]</sup> What is at first glance is simply a desire of older citizens to retire in urban surroundings, with senior friendly/accommodating characteristics, will in fact become a larger social and health policy issue relating to how society responds to the needs and influences of the growing senior population.

The trends and issues presented have international implications that are likely to increase. For example, the fastest growth segment of the North American population involves those who are 80 plus years of age. Given this, the aging baby boom cohort will likely exert significant influence on local communities, their municipal governments and the health care systems. This suggests that effective policy options will have to emerge, primarily at the municipal level, in order to reassess and redesign sometimes simple characteristics of the built environments of our cities. Overall, the intent of these policies should be to help create communities that are more vibrant and healthy for seniors as illustrated by increases in both physical and social activities of community residents.

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