Egyptian Journal of Occupational Medicine, 2013; 37 (2) : 141-156

CARDIOVASCULAR MANIFESTATIONS AMONG WORKERS IN MEAT PRODUCTION EXPOSED TO COLD ENVIRONMENT

By

[1]El Safty A, [1]Abdel Maksoud N, [2]Kandil HI and [1]Amer SS

[1]*Department of Occupational and Environmental Medicine.*

[2]*Department of Cardiology. Cairo University. Egypt.*

Abstract:

Introduction: Several mechanisms were suggested to describe the relationship between cold exposure and coronary heart disease (CHD). **Aim of the work:** Our aim is studying the prevalence of cardiovascular manifestations encountered in cold exposure and, to investigate some of the hemodynamic variables that affect the biochemical parameters especially the coagulation and the lipid profile. **Subjects and Methods:** This study was conducted on 81 subjects in one of the leading factories in meat production in Egypt and twenty subjects as control group. All the personnel were subjected to a full history taking with special questionnaire, clinical examination, and investigations involving, complete blood picture, bleeding time, plasma fibrinogen, plasma thrombin, clotting time, cryoglobulin, complete lipid profile, resting ECG and Rt.upper limb Colored Doppler. **Results:** Clinical examination showed significant prevalence in chest manifestations which was (42.2%), cardiac (47.5%) and Peripheral vascular manifestations (37.7%) among the exposed group. Investigations revealed low Hemoglobin, low platelet, low bleeding time and higher total cholesterol level among the studied groups. Cryoglobulins showed one positive case among the exposed subjects. There was a prevalence of abnormal ECG findings in 28% of the exposed group. Colored Doppler showed complete normal findings among the exposed subjects. **Conclusions and Recommendations:** We concluded that exposure to cold environment during work puts the workers in a serious risk of having clinical manifestations' changes and altered biochemical parameters in which it can lead to serious pathological disturbances. Preplacement and Periodic medical examination are recommended. Using personnel protective equipments (PPE), exposure limits schedules and establishing the work place according to the international standards of occupational health and safety is highly recommended to minimize the exposure effects.

Keywords: Cold temperature, Meat production, Bleeding time, Cryoglobulins, Colored Doppler.

Introduction

Many studies have reported an increased mortality from coronary heart disease (CHD) during the winter. Wilson et al., 2014 concluded that exposure to acute heat or cold stress elicits numerous physiological responses aiming at maintaining body temperatures. Interestingly, many of the physiological responses, mediated by the cardiovascular and autonomic nervous systems, resemble aspects of, or responses to, certain disease states. Cold stress can be experimentally used to induce stable elevations in blood pressure. Cold stress may also be used to model conditions where increases in myocardial oxygen demand are not met by anticipated increases in coronary blood flow, as occurs in older adults. Kristal-Boneh and his colleagues (1997) stated that the death rate due to cardiovascular disease including hypertension is known to be higher in winter than in summer. Observational epidemiological data in England and Wales have shown that mortality from CHD increases linearly with decrease in diurnal minimum temperature from 17 °C, accounting for about half of all excess cold-related mortality, which is approximately 50,000 per year in Britain alone (Alderson ,1985). Hong and his co-authors (2003) suggested that stroke occurrence rises with decreasing temperature.

Many authors demonstrated simultaneous elevation of blood pressure and plasma noradrenaline concentration in response to cold exposure, others found that cold-evoked sympathetic activation not only elevated blood pressure but also increased platelet count and volume and whole blood viscosity (which increased by 21%). These authors also noted a rise in cholesterol and suggested that the increase in sympathetic nervous activity related to cold may serve to enhance platelet function, offering a possible explanation for the risk to essential hypertension of thrombosis in cold weather (Arntz et al,2001 & Goodwin et al,2001). Several mechanisms have been suggested by Cook & Ubben (1990) including involvement in early atherosclerotic plaque formation, the response to endothelial damage, platelet aggregability, and increased plasma viscosity.

Indoors industries workers (meat processing industry, cold stores in industry and in the transport chain from industry to the shops) are in great risk of cold exposure. Due to the negative impact of cold on human health and performance, as well as on work productivity, quality and safety, a comprehensive strategy of risk assessment and management practices and methods is needed for work in cold environments (ISO 15743:2008).

Aim of the work: Our work is designed to study the prevalence of cardiovascular manifestations encountered among the exposed workers, to investigate some of the hemodynamic variables that affect the biochemical parameters especially the coagulation profile as well as the lipid profile, and to determine the haemostatic risk factors affecting CVS due to cold exposure. The Ultimate goal of our study is to reduce cardiovascular cold impact among cold exposed workers.

Material and Methods

This study was conducted on 81 subjects in one of the leading factories in meat production in Egypt. 61 subjects were involved in the different production sectors (55.7%) males and (44.3%) females, and referred to as exposed group. Their age ranged from 23-48 years (mean +SD 30.84+6.378). Twenty subjects were chosen as control group from other departments not exposed to same environment with matched age, sex and socioeconomic status. Their age ranged between 25-50 years (mean +SD 31.70+5.141).

All production wards including handling, separating, packaging and storing are under a temperature of 14 °C. .Some extreme of temperature exposure in the cold rooms, freezing rooms and storage room which vary the temperature between 5 °C to -45 °C. The mean duration of cold exposure was 7.26 + 3.44 years.

The studied group was subjected to a questionnaire including type of work, duration, temperature the worker is exposed to, duration of various exposures, information about personality changes, manifestations of peripheral circulatory disorders, previous attacks of ischemic heart disease, hypertension or stroke. Clinical examination was conducted to each worker at the clinic of the plant site, blood samples were taken for the following investigations:

- Complete Blood Picture.
- Lipid Profile.
- Plasma Fibrinogen.
- Plasma thrombin.
- Cryoglobulin
- Bleeding time
- Clotting time

Electrocardiogram was performed to each worker and also colored duplex for the right upper arm.

Statistical analysis:

Data were collected and analyzed using SPSS 16, the data comply with the normal distribution curve, we used the t test, chi square to analyze the data and the P value as a test of significance and < 0.05 is considered significant.

Results

Table (1) Distribution of the exposed workers according to nature of occupation (N=61)

Occupation	Frequency	(%)	Temperature range
Tunnel section	8	13.1	-45 °C
Butcher and Cutting meat	7	11.5	-18 to 1 °C
Lanshon	11	18	5-14 °C
Packing	35	57.4	10 to 14 °C

This table shows the distribution of workers according to the type of work and the environmental temperature of the different sections.

Table (2) prevalence of chest manifestations among the studied groups

Chest Manifestations	Group				X2 test	P value
	Exposed		Control			
	No	%	No	%		
Total	39	63.9%	2	10.0%	7.08	<0.05*
Chest pain	22	36.1%	1	5.0%	7.73	<0.05*
Dyspnea	17	27.9%	1	5.0%	4.55	<0.05*
Cyanosis	0	0%	0	0%		

*: Statistically significant

There is a statistically significant difference regarding chest pain and dyspnea between the exposed subjects and the control.

Table (3) the prevalence of cardiac manifestation among the studied groups.

Cardiac Manifestations	Group				X2 test	P value
	Exposed		Control			
	No	%	No	%		
Total	29	47.5%	4	20.0%	4.7	<0.05*
Palpitation	10	16.4%	3	15.0%	0.02	>0.05
Syncope	1	1.6%	0	.0%	0.333	>0.05
Fatigue	8	13.1%	3	15.0%	0.04	>0.05

*: statistically significant

There is no statistically significant difference in palpitation, syncope and fatigue between the studied groups, however, it is evident that 47% of the exposed and 20% of the control respectively, are having cardiac manifestations in which this difference shows a significant value ($P<0.05$)

Table (4) prevalence of peripheral vascular manifestation among studied groups.

Vascular Manifestations	Studied groups				X^2 value	P-value
	Exposed		Control			
	Frequency	(%)	Frequency	(%)		
Total	23	37.7	3	15	3.562	<0.05*
Reduced dexterity of hands and feet & Numbness	11	18.0	0	0	4.173	>0.05
Reduced tactile sensation	12	19.6	0	0	4.619	>0.05
Impaired ability to perceive heat, cold, and pain	0	0	0	0	0	0
Reduced joint mobility	16	26.2	0	0	6.537	<0.05*
Reduced grip strength	4	6.6	0	0	1.380	>0.05
Hypothermia	0	0	0	0	0	0
Frostbite	0	0	0	0	0	0
Pale and cold skin	7	11.5	3	15	0.173	>0.05
Uncontrollable shivering	2	3.3	1	5	0.125	>0.05
Shock	0	0	0	0	0	0

*: Statistically significant

Table (4) shows a statistical significant difference between the exposed and the control subjects as regards peripheral vascular manifestations that were prevalent among 37.7% of exposed subjects compared to 15% among controls. Also there was statistical significant higher prevalence of reduced joint motility among the studied groups.

The highest manifestations encountered among the exposed group were reduced joint motility (26.2%), followed by reduced tactile sensation (19.6) then reduced dexterity of hands, feet and numbness (18%). The higher prevalence of these manifestations among exposed group were not statistically significant compared to that of control group.

Table (5): Prevalence of CNS manifestation among studied groups:

CNS Manifestations	Studied groups				X^2 value	P-value
	Cases		Control			
	Frequency	(%)	Frequency	(%)		
Total	9	14.8	0	0	3.320	>0.05
Headache	36	59.0	0	0	21.246	<0.05*
Weakness	7	11.5	0	0	2.512	>0.05
Reduced coordination	0	0	0	0	0	0
Reduced decision-making ability	2	3.3	0	0	0.672	>0.05
Apathy or lethargy	4	6.6	0	0	1.380	>0.05
Confusion	3	4.9	0	0	1.021	>0.05
Irritability	5	8.2	0	0	1.747	>0.05
Drowsiness	2	3.3	0	0	1.021	>0.05
Loss of coordination	0	0	0	0	0	0
Slowing of breathing	0	0	0	0	0	0
Slurred speech	2	3.3	0	0	0.672	>0.05

*: Statistically significant

This table shows that headache was prevalent among 59% of the exposed subjects (statistically significant).

Table (6): Biochemical results among the studied groups:

Tested items	Groups		T-value (df=79)	P-value
	Mean ± SD			
	Cases (N=61)	Control (N=20)		
Hemoglobin	12.86±1.54	13.73±1.58	2.177	<0.05*
haematocrit	39.20±5.06	41.10±10.06	1.116	>0.05
Red cell count	4.51±0.55	4.60±0.68	0.608	>0.05
Leucocytic count	6030.33±6060.94	6060.00±1429.54	0.022	>0.05
Platelet count	158639.34±25187.98	213000.00±76698.32	4.844	<0.05*
Fibrinogen level	265.57±65.64	271.05±64.73	0.325	>0.05
C.T (lee- white)	6.56±0.87	6.90±0.91	1.515	>0.05
Bleeding Time	227.46±36.35	284.50±74.07	4.593	<0.05*
Total Cholesterol	218.20±74.42	180.45±40.37	2.160	<0.05*
T.G. 35-160 mg/dl	124.84±67.28	107.10±37.05	1.12	>0.05
HDL CHO	46.08±16.46	67.55±15.49	5.13	<0.05*
LDL CHO	147.10±68.99	114.65±32.59	2.02	<0.05*
VLDL	25.67±15.19	27.80±7.58	0.601	>0.05
Thrombin	3.97±3.18	3.95±1.28	0.023	>0.05

Cryoglobulins	Groups				X^2 test	P-value
	Cases (N=61)		Control (N=20)			
	No.	%	No	%		
3%	1	1.64	0	0%	0.332	>0.05

*: Statistically significant

Biochemical results showed a statistical significant lower level of platelets count among exposed compared to the control. However the bleeding time was statistically significant higher mainly among workers in the Lanshon section.

A statistical significant lower level of HDL was found among the exposed compared to the control (P<0.05). On the other hand, the table shows a statistically significant difference between LDL and total cholesterol among the exposed compared to control group. As for the cryoglobulins, it is evident that 1.6% of the exposed subjects were having a 3% cryoglobulins, however, there is an insignificant difference between the studied groups.

Table (7) : Lipid Profile among the studied groups in different sections:

Lipid Profile		Nº	Mean	Std. Deviation	Minimum	Maximum	P value
Total Cho.	**Lanshon**	23	186.17	44.194	125	310	>0.05
	Tunnel section	8	182.62	40.655	111	235	
	Packing	43	223.60	81.503	112	450	
	Butchera and meat Cutting	7	223.00	62.019	130	332	
	Total	81	208.88	69.345	111	450	
T.G.	**Lanshon**	23	108.74	46.343	40	240	<0.05*
	Tunnel section	8	100.62	49.817	45	200	
	Packing	43	120.26	60.728	38	320	
	Butchera and meat Cutting	7	182.86	90.685	100	360	
	Total	81	120.46	61.483	38	360	
HDL	**Lanshon**	23	59.91	19.963	25	90	<0.05*
	Tunnel section	8	40.62	16.133	25	70	
	Packing	43	48.81	16.367	20	90	
	Butchera and meat Cutting	7	51.43	22.493	25	90	
	Total	81	51.38	18.628	20	90	
LDL	**Lanshon**	23	115.35	42.724	65	255	>0.05
	Tunnel section	8	121.88	37.601	65	175	
	Packing	43	155.42	74.121	55	370	
	Butcher and meat Cutting	7	136.43	48.366	80	210	
	Total	81	139.09	63.412	55	370	
VLDL	**Lanshon**	23	29.35	12.886	13	74	>0.05
	Tunnel section	8	27.25	16.893	15	64	
	Packing	43	24.93	14.185	9	72	
	Butcher and meat Cutting	7	25.86	9.063	11	38	
	Total	81	26.49	13.645	9	74	

*: Statistically significant

This table shows a statistically significant higher level of Triglyceride(T.G) in the butcher section compared to other sections . Also it is evident that there is a statistically significant lower level high-density lipoprotein (HDL) in the tunnel section with very low temperature compared to other working places.

Our Work shows that 23% of the exposed subjects were suffering of high blood pressure. The abnormal ECG findings reported among the exposed group were manifested among 14.8% of the exposed group, while non of the control subjects suffer from ECG abnormalities. The effect of duration of exposure in years on the biochemical findings among the exposed workers showed no statistically significant difference among the studied groups.

Discussion

It is generally agreed that as temperature decreases the risk of death increases. The size of the increased risk attributable to cold temperatures seems to depend on the average annual temperature. The Eurowinter group found smaller increases in cardiovascular mortality in colder regions (Finland) than in warmer regions (Athens, Greece) (The Eurowinter Group, 1997 & Braga et al, 2003).

This study was conducted on 81 subjects in one of the leading factories in meat production in Egypt. Workers in meat processing industry are in great risk of cold exposure as temperature varied from -45 °C in tunnel section up to 14 °C in packing section. Sixty one subjects were involved in the different production sectors (55.7%) males and (44.3%) females, and referred to as exposed group. Twenty subjects were chosen as control group from other departments not exposed to same environment with matched age, sex and socioeconomic status. All the subjects were using protective equipments, however, it wasn't matching the international standards.

Our results revealed that the complaint of chest pain and dyspnea were statistically significant higher among cold exposed group. However there was no case with cyanosis in both groups (Table 2). We related the respiratory manifestations in the four different working sites and we concluded that statistically significant different prevalence of chest manifestations among the four sections with higher prevalence in the butcher and meat cutting (-18°C) with lower temperature and short duration and to a lesser extend in packing section with longer shift duration almost 12 hours. This matches with the results of Mäkinen and her colleagues (2008) who proved that cold temperature and low humidity were associated with increased occurrence of respiratory tract infections (RTIs). Also Hassi and his colleagues (2008) documented that cold causes cardiopulmonary stress often perceived as shortness of breath or chest pain, and causes exacerbation of these symptoms in persons suffering heart or lung disease.

In our study we checked the blood pressure, ECG changes as well as some cardiac symptoms as palpitation, fatigue and syncope, we found that 23% of the exposed subjects were having hypertension according to the World Health Organization criteria 1998 (systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg). Our results matched Korhonen (2006) who said that cold exposure caused a rise in systolic and diastolic blood pressures and with Huntington et al (2004) who stated that cold exposure increases the blood pressure. However, ECG revealed that 14.8% of the exposed subjects were showing abnormal readings. These findings were as follows: 1.6% showed bifasicular T wave@ lead V1,V2,V3, 3.3% showed Inverted T @III, aVF, Inverted T@Lead III, 1.6% showed prolonged P-R& Q-T interval, 1.6% showed prolonged Q-T wave, 1.6% showed prolonged P-R &Q-T interval, 1.6% showed Q wave at II, III, aVF and 1.6% showed sinus bradycardia .Lorenzo and his colleagues (1999b) found that there was a variety of cold-induced functional abnormalities such as physical performance capacity; ECG changes indicating myocardial ischemia occurring at lower loads; and possibly increased frequency of cardiac arrhythmias. We related these findings among different working sections, there was no statistically significant variation. However, 28% of the ECG abnormality was found in the butcher and meat cutting section as well as the tunnel sections in which the subjects were exposed to very low temperature.

Working in cold environments such as refrigerated warehouses, food processing facilities and outdoors in cold weather, excessive cooling of fingers and toes have been frequently reported (Sawada et al, 2001). Occupational Raynaud's phenomenon", is marked by arterial hyper-responsiveness and vasoconstriction during cold stimulation as demonstrated by Cherniak et al (2004). Madigan Medical Army Center (2007) stated in the Vascular Referral Guidelines that numbness, tingling or other sensory manifestations, and/or discomfort, generally noted in the hands or feet, also joint pain and swelling, skin tightening or thickening is initiated or aggravated by exposure to cold or damp conditions .These was in agreement with the results detected in our study (Table 4)

Vascular manifestations such as reduced dexterity of hands, reduced tactile sensation, impaired ability to perceive heat, cold, and pain, reduced joint mobility, reduced grip strength, frostbite, pale and cold skin, hotness and fever, hypothermia, uncontrollable shivering and shock were detected among our studied group. It was evident that the vascular manifestations of the exposed have statistically significant higher prevalence compared to those of the control (Table 4). Also we found four subjects having white nails and two others with clubbing.

When we related the vascular manifestations in the four different sections for the interest of more findings, we found out that although there was no statistical significant difference between the four sections, but there was a higher prevalence in butcher and meat cutting and in packing section. Our results are consistent with Rintamäki and his co-authors(1997) as their results showed that in food processing industry there are marked cold associated problems especially in the neck-shoulder area and in the hands and fingers, physical strain and fatigue.

Cold exposure may adversely affect vigilance, concentration, memory (recognition and recall), reasoning and general intelligence (Palinkas 2001and Hoffman 2001). Studying the CNS manifestation (Table 5) revealed that 59% of exposed workers were complaining of headache. It was worth noticed that there was a high prevalence in the luncheon (36.4%) and in tunnel section (25%). These results were similar to the results of Marrao et al (2005).

In our study, it was evident that there is a highly statistically significant lower level of platelet count of the exposed when compared to the non-exposed group as shown in Table(6). This matches with Lorenzo et al, 1999a in finding that exposure to cold weather, induces different haemodynamic responses and changes of blood levels of haemostatic risk factors. However, this contrasts with Spencer et al, 1998, who stated that platelet count have been shown to increase with cold weather. On the other hand, Marchant et al (1994) observed that platelet count showed no significant difference compared to the base line. When relating the platelets count according to duration of employment, it was evident that the presence of higher level in the >5 years of employment than the < of 5 years exposure but not to the level of significance. Several mechanisms have been suggested whereby raised plasma fibrinogen could produce vascular disease, including involvement in early atherosclerotic plaque formation, the response to endothelial damage, platelet aggregability, and increased plasma viscosity (Meade et al,1993).

Also Bokenes et al (2000) proved that cold exposure causes increase in hemoconcentration and an increase in the fibrinolytic parameter that initiates a mild inflammatory reaction and a tendency for an increased state of hypercoagulability. Our results (Table 6) showed lower level of fibrinogen compared to the control, however it was of no statistical significance. We have no explanation for this diversity except that more investigations are needed regarding the fibrinogen level in cold exposure. When relating the same parameter according to duration of exposure it was evident that there was an increase level of fibrinogen with>5 years exposure, which matches Woodhouse et al (1994) However it showed no statistical significance

The bleeding time showed a highly significant lower level among cold exposed workers compared to the control group. This contrasts Hata et al (1991), who found prolonged bleeding time in rodents, and Golant et al (2008) who approved the presence of severe bleeding as a bleeding disorder sign. The relation between these parameters and the duration of employment in years showed no statistical significant variation, although that there was an increase in the bleeding time for the group exposed to cold >5 years.

Immunoglobulins undergoing cold-dependent precipitation are known as cryoglobulins (Mohanty et al, 2003). Cryoglobulins are abnormal immunoglobulins that precipitate or form a gel upon exposure to cold temperatures, and initiate an inflammatory reaction similar to antigen-antibody complexes. The physical characteristic causes people with cryoglobulin to have symptoms during cold weather: blanching, numbness, and pain in their fingers or toes (Raynaud's phenomenon); bleeding into the skin; and pain in joints. People with these symptoms or any other symptoms that appear in cold weather should be tested for cryoglobulin (Gale Encyclopedia of Medicine, 2006).

We investigated presence of cryoglobulin in all exposed subjects and results revealed only one subject having this cryoglobulin (3%) matching the results of Mohanty et al(2003).

As regards lipid profile, our results showed a statistically significant higher level of total cholesterol and LDL compared to the control group. Rajender et al (2008) concluded that physical exercise in cold causes acute changes in serum lipid profile . Also Meade and his co-authors (1993), demonstrated seasonal changes in low-density-lipoprotein cholesterol (LDL cholesterol) concentration, with peak levels in winter months and increase of total cholesterol as well. This in contrast to Lorenzo et al (1998) who reported a significant reduction of total and low-density lipoprotein (LDL) cholesterol in a group of patients with hypercholesterolemia after 90 days of cold adaptation.

It is worth mentioning that for the LDL, we found two cases below normal level and other two at low normal and two cases below normal for the total cholesterol. Regarding our findings it was evident that there was an increase in triglycerides (T.G) in the exposed compared to the control, but not to the level of statistically significance. Also our results revealed a statistically significant lower level high-density lipoprotein (HDL) compared to the control group and this effect was more evident among the group of workers with duration of exposure more than 5 years. This contrasts the results of Rajender and his co-authors(2008) that revealed a significant increase in HDL and no significant changes in the total cholesterol level.

For the lipid profile, there was a high level of total cholesterol in the packing sector with low temperature and prolonged exposure, an increase in level of HDL in the butcher and meat cutting with very low temperature and continuous exposure per hour per day(-18°C). LDL showed marked decrease in the tunnel section with very low temperature and intermitted exposure duration per hour per day (-45°C) (Table 7).

Regarding the colored Doppler in the Rt.uppr limb arterio-venous, our results revealed no positive findings among the exposed group of workers.

Conclusion: Our conclusion from this study, is that the cold exposed workers in meat industry fall under serious risk that affects cardiovascular as well as central nervous systems as well as the biochemical parameter in the form of a decrease in Hb, decrease platelet count, decrease bleeding time, increase total cholesterol, increase LDL, TG, decrease HDL and a positive finding of cryogobulin.

Recommendations: The risk of cold injury can be minimized by proper equipment design, safe work practices and appropriate clothing, including gloves, insulated or vapor barrier boots, and face masks as necessary. A recommended method for protective clothing is the ventilating, insulating and protective layering (VIP) method.

For work areas below the freezing point, metal handles and bars should be covered by thermal insulating material.

Workers and supervisors involved with work in cold environments should be informed about symptoms of adverse effect exposure to cold, proper clothing habits, safe work practices, physical fitness requirements for work in cold, and emergency procedures in case of cold injury. While working in cold, a buddy system should be used. Look out for one another and be alert for the symptoms of hypothermia.

The "work warm-up schedule" developed by the Saskatchewan Department of Labor has been adopted by the American Conference of Governmental Industrial Hygienists (ACGIH) as Threshold Limit Values (TLVs) for cold stress. If the environment cannot be effectively controlled, implementation of an appropriate work/rest regime: for example, paid rest breaks of ten minutes per hour for temperatures between 9° and 7°C, twenty minutes per hour for temperatures between 7° and 4°C, and thirty minutes per hour for temperatures between 4° and 1°C (An air temperature of 1°C should be regarded as the minimum acceptable for normal work). Heated rest rooms or shelters should be provided so those workers may obtain temporary relief from the cold.

Preplacement examination should be done to exclude unfit workers. Periodic medical examination should be carried routinely to detect the early changes that may lead to health problems.

References

1. Alderson MR (1985) : Season and mortality. Health Trends; 17:8796.
2. Arntz HR, Muller-Nordhorn J and Willich SN (2001): Cold Monday mornings dangerous: epidemiology of sudden death. Curr Opin Crit Care.; 7:139-144.
3. Bokenes L, Mercer JB, MacEvilly S, Andrews JF and Bolle R (2011): Annual variations in indoor climate in the homes of elderly persons living in Dublin, Ireland and Tromso, Norway. Eur J Public Health; 21: 526-531.
4. Bokenes L , AlexandersenTE, Osterud B, TveitaT and MercerJ B (2000) : Physiological and haematological responses to cold exposure in the elderly. International Journal of Circumpolar Health; 59: 216-221.
5. Cherniack M, Clive J, and Seidner A (2004): Vibration exposure, smoking, and vascular dysfunction Clinical Testing and Management of Individuals Exposed to Hand Transmitted Vibration. An Evidence Review. Faculty of Occupational Medicine. ISBN 1 86016 203 7.
6. Cook NS and Ubben D (1990): Fibrinogen as a major risk factor in cardiovascular disease. Trends Pharmacol Sci; 11:44451.
7. Gale Encyclopedia of Medicine (2006): Mosby›s Manual of Diagnostic and Laboratory Tests. St. Louis: Mosby, Inc. Published by the Gale Group.
8. Golant A, Nord R, Paksima N, and Posner M (2008): Hand Service, Department of Orthopedic Surgery, NYUHospital for Joint Diseases, New York, NY. NYU School of Medicine. J Am Acad Orthop Surg; 16(12): 704-715.

9. Goodwin J, Pearce VR and Taylor RS (2001): Seasonal cold and circadian changes in blood pressure and physical activity in young and elderly people. Age, Ageing; 30:311-317
10. Hassi J, Remes J, Kotaniemi JT, Kettunen P and N?yh?s (2008): Dependence of cold-related coronary and respiratory symptoms on age and exposure to cold. Cold Work Action Program, Oulu Regional Institute of Occupational Health, Kastelli Research Centre, Oulu, Finland.
11. Hata T, Kawabata A, Kita T, Itoh E and Nishimura Y (1988): Changes in platelet count and related parameters in SART action of administered Neurotropin. Japan. J.Pharmacol; 47: 349-356.
12. Hong, Yun-Chul, Joung-Ho R, Lee, Jong-Tae H, Eun-Hee K, Ho-Jang S and Kim, H P (2003): Ischemic stroke associated with decrease in temperature. Epidemiology; 14(4):473-478.
13. ISO 15743(2008): Ergonomics of the thermal environment Cold workplaces Risk assessment. www.iso.org
14. Korhonen I (2006): Blood pressure and heart rate responses in men exposed to arm and leg cold pressor tests and whole-body cold exposure. Int J Circumpolar Health. ; 65(2):178-84.
15. Kristal-Boneh E, Harari G and Green MS (1997): Seasonal change in 24-hour blood pressure and heart rate is greater among smokers than nonsmokers. Hypertension; 30: 436441.
16. Lorenzo F, Sharma V, Scully M and Kakkar V (1999): Cold adaptation and the seasonal distribution of acute myocardial infarction, the Thrombosis Research Institute, London, SW3 6LR UK. J Med; 92: 747-751.
17. Lorenzo F, Mukherjee M, Sherwood R, Kadziola Z and Kakkar VV (1998): Central cooling effects in patients with hypercholesterolaemia. Thrombosis Research Institute, Emmanuel Kaye Building, Manresa Road, Chelsea, London SW3 6LR, U.K., and Department of Biochemistry, King's College Hospital, Denmark Hill, London SE5 9RS, U.K. Clinical Science; 95: 213-217.
18. Madigan Medical Army Center (2007): www.mamc.amedd.army.mil/Referral/guidelines/vascular_coldweather.htm
19. Mäkinen TM, Juvonen R, Jokelainen J, Harju TH, Peitso A, Bloigu A, Silvennoinen-Kassinen S, Leinonen M, Hassi J (2009): Cold temperature and low humidity are associated with increased occurrence of respiratory tract infections.
20. Respir Med ;103(3):456-62. doi: 10.1016/j.rmed.2008.09.011. Epub 2008 Nov 1.
21. Marchant B, Donaldson G, Mridha K, Scarborough M and Timmis A(1994): Mechanisms of cold intolerance in patients with angina. J Am Coll Cardiol; 23:6306.
22. Marrao C, Tikuisis P, Keefe A, Allan A, Valerie G and Gordon G. (2005): Physical and Cognitive Performance during Long-Term Cold Weather OperationsAviation, Space, and Environmental Medicine; 76 (8): 744-752.
23. Meade TW, North WRS, Chakrabarti RR, Stirling Y, Haines I, and Thompson SG (1980): Haemostatic function and cardiovascular death: early results from a prospective study; Lancet; i: 10504.
24. Mohanty S, Jayawardhana R, Huilamo N and Mamajek E (2007): The Planetary Mass Companion 2MASS 12073932B: Temperature, Mass, and Evidence for an Edge-on Disk. The Astrophysical Journal; 657:1064-1091
25. Mohantya S, Weinerb SM, Mentelec R, Vaithb P, Lottspeichd F and Illges H. (1994): Immunology, Department of Biology, Faculty of Sciences, University of Konstanz, Germany. Department of Rheumatology and Clinical Immunology, Albert-Ludwigs University Medical Center, Freiburg, GermanyAbteilung flr Klinische Chemie und Klinische Biochemie in der Chirurgischen Klinik und Poliklinik-Innenstadt, Ludwig-Maximillians-Universität
26. Palinkas LA, Mäkinen TM, Pääkkänen T, Rintamäki H, Leppäluoto J and Hassi J (2005): Influence of seasonally adjusted exposure to

cold and darkness on cognitive performance in urban circumpolar residents. Scand J Psychol; 46: 239-246.

27. Rajender K, Gaurav T and Jaspal SS (2008): Comparison of the acute effect of single session of submaximal exercise in hot and cold ambient temperatures on lipid profile .Department of sports Medicine and Physiotherapy, Guru Nanak Dev University, Amritsar cold exposure injuries to the extremities, No. 704-715.The American Academy of Orthopaedic Surgeons.
28. Rintamki H, Korhonen E, Rissanen S, Oksa J and Pienim?ki T (1997): Cold problems and upper limb muscular strain in food processing industry, Oulu Regional Institute of Occupational Health, Oulu, Finland.
29. Sawada S, Araki S, Yokoyama K and Sato H (2001): Effect of clothing on cold-induced vasodilatation (CIVD) response and subjective thermal loads during repeated finger cooling. Proceedings of the Australian Physiological and Pharmacological Society 32 (2), 137P.
30. Spencer FA, Goldberg RJ, Becker RC and Gore JM (1998): Seasonal Distribution of Acute Myocardial Infarction in the Second National Registry of Myocardial Infarction. J Am Coll Cardiol; 31:122633.
31. Wilson T, Klabunde R and Monahan K (2014): Using Thermal Stress to Model Aspects of Disease States. J. thermal biology. http://dx.doi.org/10.1016/j.jtherbio.2014.03.003
32. Woodhouse PR, Khaw KT, Plummer M, Foley A and Meade TW (1994): Seasonal variations of plasma fibrinogen and factor VII activity in the elderly: winter infections and death from cardiovascular disease. Lancet; 343:4359.
33. Workplace Amenities and First Aid (2008) http://www.worksafe.vic.gov.au/wps/wcm/connect/WorkSafe/Home/Forms.