Relation of haemostatic function, neurovascular impairment, and vibration exposure in workers with different stages of vibration induced white finger

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ABSTRACT Haemostatic function and neurovascular symptoms were investigated in 67 workers exposed to vibration and 46 comparable referents. Of these 65.6% of vibration workers complained of neurological disturbances (stages 0_T, 0_N of Taylor's classification for vibration induced white finger (VWF) and 20.9% suffered from Raynaud's phenomenon (stages 1-2-3). The severity of the staging symptoms showed a close relation with an index of vibration dose computed on the basis of vibration measurement and individual exposure time. Indices of platelet aggregation, both in vitro and in vivo, antithrombin III, fibrinogen and fibrinopeptide A levels were not different in the exposed workers compared with the referents. No relation was found between haemostatic parameters and the severity of VWF. Exposed workers responded to a cooling procedure with a more pronounced vasoconstriction in the digital vessels than the referents, as indicated by delayed recovery time of finger skin temperature after the cold test. These findings suggest that both in the early stages (0_T, 0_N) and in more severe stages of VWF (stages 1-2) cold induced hyperreactivity in the digital vessels and Raynaud's syndrome are vascular disorders of functional origin occurring without any prethrombotic alterations.

Abnormal haemostatic function has been reported in primary Raynaud's disease and in secondary Raynaud's phenomenon.¹ Zahavi *et al* found that platelet aggregation induced by adenosine-diphosphate (ADP) and beta-thromboglobulin were higher in patients suffering from Raynaud's phenomenon than in referents.² Lower threshold concentration for ADP induced platelet aggregation was reported by Blunt *et al* in female patients with Raynaud's syndrome compared with referents.³ Some authors have suggested that platelet abnormalities might be involved in the pathogenesis of the digital vasospasm,⁴ but whether platelet disorders are the cause or the effect in the peripheral vasospastic syndrome is still unknown.

Raynaud's phenomenon is the most important component of vibration syndrome, which includes the complex of osteoarticular, neurological, and vascular lesions occurring in the hands of workers exposed to hand-arm vibration. Among the

pathogenic theories on the onset and perpetuation of Raynaud's phenomenon of occupational origin, one emphasises the role of endothelial injury secondary to enhanced arterial wall shear stress induced by the excessive mechanical energy entering the fingers of subjects who use handheld vibratory tools.⁵ As a consequence, haemostatic disorders might be observed in vibration exposed workers affected with peripheral vasospastic symptoms. Few reports exist on this topic. Both generic hypocoagulability,⁶ and a tendency to hypercoagulability as indicated by increased fibrinogen concentration⁷ and a shortening of the heparin thrombin clotting time³ have been reported in workers with Raynaud's phenomenon. In patients exposed to hand-arm vibration for a long time in vitro platelet aggregation indices were found to be higher than in normal subjects.⁸ In a previous report we failed to observe a significant difference in platelet function tests and clotting parameters between 22 vibration exposed workers and 20 comparable referents.⁹ Among the exposed workers, however, only one man suffered from vibration induced

white finger (VWF), the others having no symptoms or neurological disturbances.

The purpose of the present study was to investigate the relation among haemostatic function, neurovascular symptoms, and vibration exposure in a larger sample of exposed workers at different stages of vibration induced white finger.

Materials and methods

SUBJECTS

Sixty seven operators using pneumatic chipping and grinding tools at a large grey iron foundry were examined. Health status and occupational histories were collected by a standardised questionnaire administered by trained nurses. Neurological and vascular symptoms in the fingers, such as tingling, numbness, and blanching, were classified according to the stage system for VWF described by Taylor *et al.*¹⁰ The workers were also questioned as to their use of tobacco and alcohol. A general clinical examination was carried out by two physicians who carefully examined the target organs affected by exposure to vibration and confirmed the stage assessment for VWF. Exposure time to segmental vibration was estimated both as hand tool usage years and as total working hours¹¹ because of the difference in daily exposure time (h) among the vibration workers.

Forty six healthy men working at the foundry and not exposed to vibration formed the reference group. They were submitted to the same medical procedure, laboratory investigations, and circulatory function test as the exposed workers.

COLD PROVOCATION TEST

To assess peripheral vascular function, a cold test was performed on the right hand of the referents and the exposed workers. Skin temperature was measured on the dorsal surface of midphalanx of the third right finger before and after immersion of the hand in cold water (4°C) for two minutes. A thermistor probe (LSI, Milan, Italy) was used for skin thermometry. The rewarming time of the finger was evaluated by monitoring skin temperature every three minutes during the first 30 minutes after the cooling period. The cold test was carried out at room temperature of 22.5°C (SD 0.4°C).

LABORATORY DATA

Platelet function and clotting parameters were studied in all 113 subjects. Venous blood collection was performed in the early morning using a non-occlusive technique. Venous samples were withdrawn after an overnight fast, after 12 hours of smoking abstinence, and after abstention from anti-

platelet drugs for at least 10 days.

PLATELET AGGREGATION

Platelet aggregation was performed according to Born's photometric method.¹² The blood sample (18 ml) was withdrawn into a plastic syringe containing 2.0 ml of 3.8% sodium citrate. Platelet rich plasma was prepared by centrifuging the citrated blood into plastic tubes at 400 rpm and counted by an automatic platelet counter (ULTRA FLO 100). Platelet aggregation was determined by a photometer ELVI 840 assuming the transmittance of platelet poor plasma as 100% of aggregation. The sample, adjusted to contain 300–350 000 platelet/mm³, was tested with adrenaline at 4.0 µM and with ADP at 0.8 µM. The transmittance value (%) after five minutes of platelet aggregation was assumed. The ADP threshold concentration inducing the release reaction was also determined.

BETA-THROMBOGLOBULIN

The blood was collected using evacuated glass tubes (Abbott)¹³ containing 2.5% ethylenediaminetetraacetate, 0.025% chloradenosine, and 7% procaine-hydrochloric acid. Beta-thromboglobulin levels were assayed using the Amersham Ria Kit according to Ludlam *et al.*¹⁴

PLATELET FACTOR FOUR

Platelet factor four levels were assayed with the use of the Abbott Ria Kit. The collection and preparation of the samples were the same as previously described for beta-thromboglobulin.

PLATELET FACTOR THREE

This was considered as Stypven time¹⁵ and performed on platelet rich plasma by a semiautomatic instrument (Fibrintimer Labor).

FIBRINOPEPTIDE A

Fibrinopeptide A was assayed using the Mallinckrodt Kit according to Nossel *et al.*¹⁶

ANTITHROMBIN III

Antithrombin III was determined by chromogenic substrate (Abbott Kit).¹⁷

Platelet count, fibrinogen, total and high density lipoprotein cholesterol, triglycerides, and immunoglobulins G, A, and M were also determined in the exposed and reference workers.

VIBRATION MEASUREMENT AND VIBRATION DOSE

Vibration measurements were made at the work site, and two skilled operators were requested to use the vibrating tools under normal working condi-

tions. Vibrating handheld tools consisted of a pneumatic chipping hammer and a straight grinder. A delta shear type accelerometer (B&K 4367) and a shock accelerometer (B&K 8309) were rigidly fastened to the handles of the grinder and chipping hammer. The signal from the transducers was fed into charge amplifiers (B&K 2635) and recorded on a FM tape recorder (B&K 7003). Vibrations were measured in the three axes X, Y, Z with a frequency range from 0.2 Hz to 3000 Hz. One third octave band frequency spectra of the recorded vibration signals were obtained in the laboratory using a digital frequency analyser (B&K 2131) connected to a graphics recorder (B&K 2313). The magnitude of the vibration at each 1/3 octave centre frequency from 6.3 Hz to 1250 Hz was calculated as acceleration level in decibels:

$$L_h = 20 \log (a/a_0) \quad (\text{dB})$$

where a = rms acceleration in m/s^2 and a_0 = reference acceleration of 10^{-6}m/s^2 .

From the results of the frequency analysis, the weighted acceleration level (L_{hw}) of vibration was computed using the frequency weighting factors and the equation proposed by ISO/DIS 5349.¹⁸

Table 1 gives the weighted acceleration levels measured in three orthogonal axes of the vibrating tools.

According to the method specified in ISO/DIS 5349,¹⁸ the daily exposure to vibration for each foundry worker was characterised in terms of four hour energy-equivalent frequency weighted acceleration level, $(L_{hw})_{eq}^{t=4}$, by the formula:

$$(L_{hw})_{eq}^{t=4} = (L_{hw})_{eq}^{t=1} + 10 \log (t/4) \quad (\text{dB})$$

where $(L_{hw})_{eq}^{t=1}$ is the equivalent frequency weighted acceleration level for a daily exposure of t hours.

On the basis of duration of exposure to vibration (years), a vibration exposure level (VEL) was also computed for each operator. This index represents the total energy level entering the fingers and the hands of the workers exposed to vibration over a specified period. The vibration exposure level was calculated as follows:

$$\text{VEL} = (L_{hw})_{eq}^{t=4} + 10 \log (T/T_0) \quad (\text{dB})$$

where T is the total exposure time in years and T_0 a reference year that comprises 240 days of vibration exposure.

STATISTICAL METHODS

Student's t test, chi square test, and bivariate correlation and linear regression analyses were used for statistical evaluation of the data. A probability level of 0.05 was stated as the limit of statistical significance.

Results

PREVALENCE OF SYMPTOMS AND VIBRATION EXPOSURE

The information derived from the questionnaire and the medical interview were used for staging the neurological and vascular symptoms according to Taylor's classification. Of the 67 workers exposed to vibration, nine (13.4%) had no disturbances (stage 0) and 44 (65.6%) complained of neurological symptoms; among these latter, 31 (46.2%) were affected by tingling (stage 0_T) and 13 (19.4%) by numbness (stage 0_N) in the fingers. The remaining 14 foundry workers (20.9%) suffered from Raynaud's phenomenon of occupational origin: nine workers were in stage 1 (13.4%), four in stage 2 (5.9%), and one in stage 3 (1.5%). Among the workers with white fingers, the right hand was more affected (85.7%) than the left (57.1%); six men (42.8%) reported vasospastic attacks in both hands. The highest prevalence of blanching symptoms occurred in the third right (57.1%) and left (42.8%) fingers. Neurological disturbances were present in all the workers with vasospastic syndrome. None of the 46 referents was found to be suffering from Raynaud's phenomenon or disease and only two men complained of paresthesia in the fingers.

Table 2 gives the age, exposure time, and vibration exposure level of the foundry workers. Foundry workers affected with Raynaud's phenomenon were older than the other exposed workers. Exposure to vibration expressed both as working time (years and total hours) and as vibration exposure level (dB) was significantly higher in the workers with vascular symptoms than in those with no symptoms or with

Table 1 Weighted acceleration levels (L_{hw} in dB) measured at the handle of vibrating tools in three orthogonal axes X, Y, Z

Tools	Centre frequency (Hz)	Weighted acceleration level (dB*)		
		$L_{hw} (x)$	$L_{hw} (y)$	$L_{hw} (z)$
Chipping hammer	31.5	149	146	150
Straight grinder	125	139	137	138

*dB re 10^{-6}m/s^2 .

Table 2 Age, exposure time, and vibration dose in the vibration exposed workers. Values are given as mean (SD)

Characteristics	Stages of vibration induced white finger			
	Stage 0 (n = 9)	Stages 0 _T -0 _N (n = 44)	Stages 1-2-3 (n = 14)	Total (n = 67)
Age (years)	38.8 (7.3)	38.5 (7.6)	43.7 (5.4) [^]	39.6 (7.3)
Duration of exposure (years)	5.6 (4.5)	9.1 (5.8)	16.5 (6.0)**	10.2 (6.6)
Total working time (hours)	2056 (1405)	3629 (2423)	10978 (5604)**	4953 (4501)
Vibration exposure level (dB)	144 (6.5)	151 (5.1)**	157 (3.3)**	151 (6.1)

Significant from stage 0: * p < 0.001; ** p < 0.01.

Significant from stages 0_T-0_N: ° p < 0.005; ^ p < 0.025.

neurological complaints alone. The relation between vibration exposure level and severity of the staging symptoms of VWF is evident from table 3. The mean and median latencies of blanching for workers with stages 1-2-3 were 9.2 years (SD 6.8) and 8.0 years (range 2-25) respectively. The latent period is here considered as exposure time before the onset of finger blanching.

PLATELET FUNCTION AND COAGULATION PARAMETERS

In table 4 the main characteristics of the workers exposed to vibration are compared with those of the referents. No difference was found between the referent group and the entire exposed population.

Nevertheless, when the vibration workers were subdivided into different stages of VWF, subjects with blanching symptoms showed a significantly higher diastolic blood pressure and total cholesterol level than the referents and the other exposed workers. The diastolic arterial pressure and total cholesterol levels correlated well with the age of all subjects ($r = 0.38$, $p < 0.001$).

Table 5 shows the results of the platelet functions tests and the clotting assays. Indices of platelet aggregation both in vitro and in vivo, antithrombin III, fibrinogen, and fibrinopeptide A levels did not differ significantly in the exposed workers at different stages of VWF compared with the referents. No relation was found between the haemostatic para-

Table 3 Vibration exposure level and severity of symptoms in the fingers of foundry workers using chipping and grinding tools. Values are given as numbers (%)

Stages of vibration white finger	Vibration exposure level		
	≤145 dB	146-155 dB	≥156 dB
Stage 0 (n = 9)	6 (8.9)	3 (4.5)	—
Stages 0 _T -0 _N (n = 44)	5 (7.5)	29 (43.2)	10 (14.9)
Stages 1-2-3 (n = 14)	—	2 (3.0)	12 (17.9)
Total (n = 67)	11 (16.4)	34 (50.7)	22 (32.8)

Chi square value: 39.2 ($p < 0.0005$).

Table 4 Age, anthropometric data, smoking and alcohol habits, blood pressure, and serum lipid concentrations in referents and vibration exposed workers. Values are given as mean (SD)

	Referents (n = 46)	Chipping and grinding operators			
		Stage 0 (n = 9)	Stages 0 _T -0 _N (n = 44)	Stages 1-2-3 (n = 14)	Total (n = 67)
Age (years)	39.6 (7.2)	38.8 (7.3)	38.5 (7.6)	43.7 (5.4)**	39.6 (7.3)
Body surface area (m ²)	1.96 (0.15)	1.93 (0.09)	1.93 (0.14)	1.93 (0.09)	1.93 (0.12)
Cigarette consumption (total packets)	4785 (4,543)	4156 (4,232)	3888 (4,056)	2495 (3,454)	3633 (3,949)
Alcohol (g/d)	40.6 (26.4)	43.3 (29.2)	48.9 (33.3)	35.2 (14.9)	45.3 (30.1)
Systolic arterial pressure (mm Hg)	130 (12.8)	127 (7.9)	127 (12.8)	135 (16.9)	129 (13.4)
Diastolic arterial pressure (mm Hg)	82.5 (10.2)	81.1 (6.5)	84.3 (9.7)	88.9 (8.5)*	84.8 (9.3)
Total cholesterol (mg/dl)	228 (48.9)	202 (32.1)	223 (53.3)	265 (52.8)**	229 (54.1)
High density lipoprotein cholesterol (mg/dl)	54.2 (19.8)	48.6 (19.7)	50.2 (9.1)	55.7 (10.1)	50.6 (11.1)
Triglycerides (mg/dl)	141 (95.1)	118 (61.0)	114 (58.1)	110 (54.1)	114 (56.8)

Significant from referents: *p < 0.05; **p < 0.025.

Table 5 Platelet count, in vitro and in vivo platelet aggregation indices, and blood coagulation parameters in referent and vibration exposed groups. Values are given as mean (SD)

	Referents (n = 46)	Chipping and grinding operators			
		Stage 0 (n = 9)	Stages 0 _T -0 _N (n = 44)	Stages 1-2-3 (n = 14)	Total (n = 67)
Platelet count ($\times 10^3/\text{mm}^3$)	235 (52.1)	213 (38.5)	238 (62.2)	231 (77.9)	233 (60.6)
A ₂ adenosine-diphosphate (%)	42.3 (25.9)	52.2 (18.2)	55.4 (66.6)	45.0 (34.0)	50.3 (57.2)
A ₂ epinephrine (%)	45.1 (20.9)	47.2 (10.8)	40.5 (22.5)	42.2 (29.4)	42.0 (21.5)
Adenosine-diphosphate (threshold) ($\times 10^{-6}\text{M}$)	0.79 (0.90)	0.74 (1.11)	0.99 (1.01)	1.02 (0.60)	0.97 (0.97)
Platelet factor three/platelet rich plasma (s)	46.7 (11.1)	53.0 (9.1)	50.8 (7.5)	48.9 (13.0)	51.0 (8.4)
Platelet factor four (ng/dl)	15.8 (14.0)	12.3 (3.6)	11.6 (9.2)	16.5 (19.7)	14.2 (10.35)
Beta-thromboglobulin (ng/dl)	55.1 (31.0)	36.7 (6.9)	42.6 (25.6)	56.4 (36.6)	47.7 (25.5)
Antithrombin III (%)	100 (14.2)	106 (19.9)	107 (17.6)	101 (17.8)	106 (17.6)
Fibrinogen (mg/dl)	244 (88.4)	260 (41.9)	235 (46.1)	245 (27.6)	241 (43.3)
Fibrinopeptide A (ng/ml)	5.4 (3.3)	5.8 (3.1)	6.6 (3.3)	5.7 (3.8)	6.2 (3.5)

meters and the stages of vibration syndrome or between the haemostatic parameters and the duration of exposure to vibration.

PERIPHERAL CIRCULATORY FUNCTION

Figure 1 displays the results of the cold provocation

test performed on the right hand of the referent and exposed groups. At rest, the mean skin digital temperature was lower in the workers affected by white finger than in the referents ($p = 0.016$). Local cooling induced blanching of the fingers in six of the 14 subjects (42.8%) suffering from Raynaud's

Fig 1 Digital skin temperature curves during first 30 minutes after cold test in referents and workers exposed to vibration subdivided into different stages of VWF. Plotted values represent means and standard errors of means. Significant from referents: (A) Stages 0_T-0_N: 3 min $p = 0.019$, 6-30 min $p < 0.001$. (B) Stages 1-2-3: at rest $p = 0.016$, 3 min $p < 0.005$, 6-30 min $p < 0.001$.

Fig 2 Correlation between vibration exposure level and total working time in workers exposed to vibration.

phenomenon. The monitoring of skin temperature of the third right finger after cold stimulation showed that the rewarming rate was significantly slower in the exposed workers with neurological (stages 0_T, 0_N) and vascular (stages 1–2–3) symptoms than in the referents ($p = 0.019 - 0.0001$). The temperature curves indicate that the more severe the vibration syndrome, the lower the digital skin temperature at each time of the rewarming period, even if the differences were not significant.

Discussion

In the present study the severity of neurological and vascular symptoms of chipping and grinding operators showed a strong dependence on occupational exposure to vibration. There was evidence for a significant relationship between the stages of VWF and the vibration dose. No foundry worker affected with Raynaud's phenomenon had worked with vibrating tools for less than 3500 hours nor had he been exposed to a cumulative weighted acceleration level of less than 148 dB. Total working hours and vibra-

tion exposure levels were good indices of vibration dose and correlated well (fig 2). These findings agree with those of other studies which have reported a direct association between exposure time and the severity of vibration syndrome.^{11 19 20}

The laboratory investigations showed that no anomalous changes in haemostatic function could be shown in the chipping and grinding workers when compared with the referents. Neither in vitro platelet aggregation induced by adenosine-diphosphate and adrenaline nor specific markers of in vivo platelet release reaction (beta-thromboglobulin and platelet factor four) were found to differ among the referents or exposed workers subdivided into various stages of VWF. Assays of other important parameters of blood coagulation such as antithrombin III and fibrinopeptide A indicated that in vivo clotting control and thrombin activity were also normal in both groups.

Platelet disorders have been reported in patients suffering from Raynaud's phenomenon not due to the use of vibrating tools.¹³ Endothelial damage is considered to be the primary event for in vivo platelet activation and for the development of thrombotic processes. In patients affected with collagen disease a vasospastic syndrome and platelet abnormalities are often associated with immunological alterations such as an increase in serum immunoglobulins.^{21 22} The normality of our haemostatic and immunological data (tables 5 and 6) indicate that in the exposed workers mechanical vibration neither provokes injury to the endothelial layer of arterial wall nor induces changes in humoral immunity.

As finger skin temperature is related to total digital blood flow,^{23 24} curve patterns of temperature recovery time after the cold test indicate that in exposed workers digital arteries responded to local cooling with a more pronounced vasoconstriction than in the referents. Among the chipping and grinding operators, moreover, the release of arterial vasospasm after the cooling procedure was slower in those subjects suffering from Raynaud's phenomenon than in those with no symptoms or with neurological disturbances alone. Studying the effects of vibratory stimulation on the femoral arteries of

Table 6 Concentration of serum immunoglobulins (Ig) in referents and vibration exposed workers. Values are given as mean (SD)

	Referents (n = 46)	Chipping and grinding operators			
		Stage 0 (n = 9)	Stages 0 _T –0 _N (n = 44)	Stages 1–2–3 (n = 14)	Total (n = 67)
IgG (mg/dl)	1166 (210)	1193 (352)	1170 (155)	1164 (168)	1172 (191)
IgA (mg/dl)	242 (91)	252 (82)	256 (96)	254 (69)	255 (89)
IgM (mg/dl)	124 (51)	118 (93)	146 (69)	155 (54)	144 (70)

dogs and rats, Azuma *et al* have shown that vibration induced hyperresponsiveness of the arterial smooth muscles to noradrenaline.²⁵ These experiments support the opinion that hyperreactivity of the digital vessel observed in workers exposed to vibration may be due to a local vibratory stress that enhances the responsiveness of the arterial muscular wall to sympathetic stimuli such as loud noise or cold.^{26,27}

The findings of the present study extend our previous suggestions⁹—that is, that not only in the early stages (0_T , 0_N) but also in the more severe stages of VWF (stages 1–2) both cold induced hyperreactivity in the digital vessels and Raynaud's syndrome are vascular disorders of functional origin occurring with no prethrombotic alterations.

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