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Field Study

Plasma Concentration of Adrenocorticotropic Hormone in Traffic Policemen

Francesco TOMEI[1], Maria Valeria ROSATI[1], Tiziana Paola BACCOLO[1], Andrea BERNARDINI[1], Manuela CIARROCCA[1] and Enrico TOMAO[2]

[1]University of Rome "La Sapienza", Department of Occupational Medicine and [2]Center For Aeromedical Evaluation and Occupational Medicine IML, ITAF, Italy

Abstract: Plasma Concentration of Adrenocorticotropic Hormone in Traffic Policemen: Francesco TOMEI, *et al*. University of Rome "La Sapienza", Department of Occupational Medicine— The aim of this study is to evaluate whether traffic policemen exposed to urban pollutants and possible psycho-social stressors could be at risk of changes on plasma adrenocorticotropic hormone [ACTH(P)] levels compared to a control group. Traffic policemen were matched by sex, age, length of service and drinking habit (<50 g of wine or beer per day) with a control group after excluding principal confounding factors; 62 traffic policemen with outdoor activity (34 men and 28 women) and 62 control subjects with indoor activity (34 men and 28 women) were included in the study. The levels of ACTH(P) were significantly higher in male and female traffic policemen than in the control subjects (respectively P=0.040, P=0.043). The authors hypothesise that occupational exposure to chemical and physical stressors, that may interact with possible psycho-social stressors, could cause a change in ACTH(P) levels in traffic policemen.
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Key words: ACTH(P), Urban pollutants, Traffic policemen, Stressors, Outdoor activity

The main agents of atmospheric pollution are vehicles with internal combustion engines, industries, thermoelectric power stations, fuels for domestic heating, and waste incineration, especially if this is carried out without a proper plan for keeping down the dusts and purifying the fumes. Urban pollution is brought about principally by motor traffic and domestic heating. These pollutants are either not present or are present at a lower level of concentration, and may produce toxic effects on human beings, animals, vegetation or materials.

The adrenocorticotropic hormone (ACTH) is a protein neurohormone produced by corticotropic cells of the anterior pituitary gland that promotes secretion of steroidal hormones by the adrenal cortex.

Scientists who have done studies on animals and human subjects have proposed that urban pollutants may cause an increase in ACTH(P) levels. Carbon monoxide[1)], benzene and toluene[2)] increase ACTH. On the other hand, cadmium[3–5)], mercury and copper[5)] cause a decrease in ACTH(P) levels. Physical agents such as noise[6–8)] and psycho-social stressors[9–14)] also increase concentrations of ACTH(P).

The workers examined in this study were employees of the Municipal Police of a big Italian city, whom we have already studied in previous studies, the environmental and biological levels of some urban pollutants[15–18)]. Exposure dosage to benzene was (mean 7 h) 10.7 μg/m^3 for traffic policemen but about three times lower (3.6 μg/m^3) in controls[15, 16)]. Although unleaded petrol had been introduced, a mixed system existed in Italy at the time of this study (use of leaded and unleaded petrol). Moreover, it is probable that anti-detonation additives containing manganese and nickel are present in fuels. The use of unleaded petrol may be the cause of the increase in benzene in the urban atmosphere.

In the period March-April 2001, the Municipality of the city in question monitored concentrations of particulate matter 10 micrometers in diameter and smaller (PM10), considered inhalable, in fixed stations located in districts with different intensities of traffic, registering mean monthly values respectively of 60 μg/m^3, 45 μg/m^3 and 30 μg/m^3 in a municipal park (http://www.comune.roma.it).

The aim of this study is to evaluate whether traffic policemen exposed to urban pollutants that may interact with possible psycho-social stressors, could be at risk of changes in ACTH(P) levels compared with a control group.

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Correspondence to: F. Tomei, Via Monte delle Gioie No. 13, 00199 Rome, Italy

Table 1. Age, Length of service, ACTH(P) concentrations in male and female workers (traffic policemen and controls)

	Male workers (n=68)						Female workers (n=56)					
	Traffic Policemen (n=34)			Controls (n=4)			Traffic Policemen (n=28)			Controls (n=28)		
Parameters	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
Age (yr)	45.9	5.8	34–56	46.2	5.1	34–55	38.9	4.6	33–51	38.7	4.6	32–49
Length of service (yr)	10.2	4.8	1–23	10	4.3	2–21	7.5	4.8	1–18	7.1	4.1	1–17
ACTH(P) (pg/m*l*)	17.7*	6.1	10.3–40	15*	4.4	9.2–23.1	17.2**	6	7.4–34	14.4**	3.9	7.8–24.9

Notes: P=plasma, SD=standard deviation, *Male Traffic Policemen vs. male controls; p=0.040, **Female Traffic Policemen vs. female controls; p=0.043

Materials and Methods

The research was carried out on a working population of 395 Municipal Police employees.

Two groups were studied: traffic policemen who worked in shifts on parking, patrols, keeping passageways free, controlling traffic at crossings and on roads with intense flows of traffic; and subjects who carry out indoor activities of an administrative and bureaucratic nature, used as control group at a lesser level of exposure. Traffic policemen and the control group worked for seven hours a day at least five days a week.

For inclusion in the study, all workers were given a questionnaire covering the following: age, length of service, pharmacological therapies, use of paints, pesticides and solvents during time off, cigarette smoking habit (mean number of cigarettes smoked, years of subjection to the habit), drinking habit (wine, beer, spirits; number of glasses of wine, beer or spirits drunk per day), clinical symptoms.

In order to avoid the influence of confounding factors, subjects who regularly made use of oral contraceptives[19–21], and those who had continual exposure to solvents, paints and pesticides[22–24] were excluded from the study. Also the subjects with a cigarette smoking habit have been excluded from the study because it has been reported that within 10 min after smoking two cigarettes the plasma ACTH level increases[25]. Subjects who referred to habitual consumption of spirits were not included in the study. Subjects excluded from the study ingested ≥50 g of ethanol per day (more than 2 glasses of wine or beer per day), a dose that alters the plasma ACTH level[26].

Subjects included in the study ingested <50 g ethanol per day (less than or equivalent to 2 glasses of wine or beer per day), a dose that does not alter the plasma ACTH level[27, 28].

Nevertheless, traffic policemen were matched with controls (mean, SD, distribution) by drinking habit (<50 g of wine or beer per day) to avoid that individual susceptibility to alcohol could alter ACTH(P) levels[26–32].

All the subjects included or excluded from the study were asymptomatic.

Traffic policemen were matched with controls (mean, SD, distribution) by sex, age, length of service and drinking habit (<50 g of wine or beer per day). Thus, sixty-two traffic policemen exposed to urban pollutants (34 men and 28 women) and sixty-two controls with indoor activity (34 men and 28 women) were included in the study.

The characteristics of the study population are shown in Table 1. Age was not less than 32 yr and not more than 56 yr both for the traffic policemen and controls of both sexes. Subjects who had been working for less than 1 yr were not included in the study. Working life was not longer than 23 yr for both the traffic policemen and the controls of both sexes, since there were no workers with longer service in our sample.

All of the subjects consented to their personal details being available, declaring that they had been made aware that these data are ranked as "sensitive information", and consented that the data arising from the research protocol should be treated in an anonymous and collective way, with scientific methods and for scientific purposes in accordance with the principles of the Declaration of Helsinki.

A 10 m*l* sample of venous blood was taken from each worker between 8 and 10 a.m., fasting. The blood samples were preserved at the place of work in a refrigerator at –4°C until the time when they were transferred (by means of a container and at the same temperature) to the laboratory, where they were immediately centrifuged to obtain the serum that was preserved at –20°C until the time when they were analysed (within 3 d). The samples were taken in the period from 14th March to 20th April 2001.

The analysis laboratory executed dosing of ACTH(P) on samples of venous blood by means of immunoradiometric assay (IRMA): our laboratory's normal values are 7.0–50 pg/m*l* for both sexes. The IRMA method which overcomes most limitations of earlier methods, has high accuracy and specificity, and is a useful and

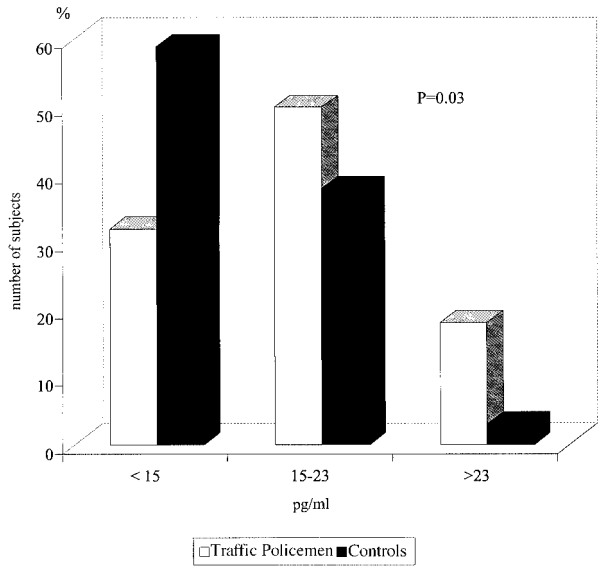

Fig. 1. distribution of ACTH (P) values (pg/m*l*) in traffic policemen and controls (%) of male sex.

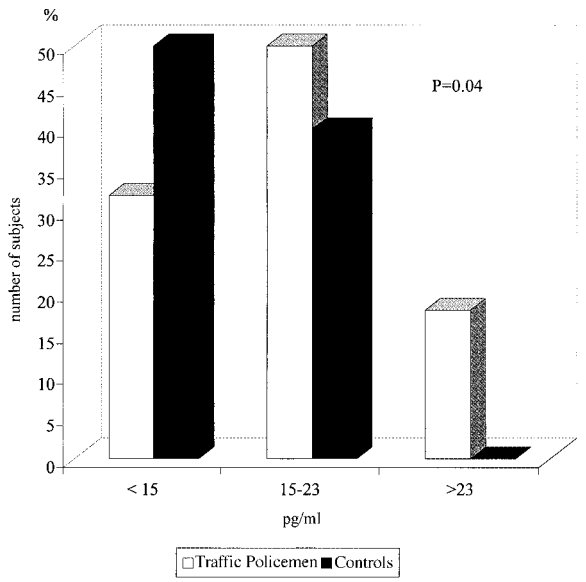

Fig. 2. distribution of ACTH (P) values (pg/m*l*) in traffic policemen and controls (%) of female sex.

convenient system for quantifying ACTH(P)[33, 34].

The laboratory did not know which samples came from the group of traffic policemen and which from the unexposed group, although both the physicians and the technicians knew how the study was being carried out.

Statistical Analysis

Statistical analysis of the data was based on the calculation of the mean, standard deviation, distribution, range and frequency according to the nature of the single variables. The differences between the means were compared by using Student's t test for unpaired data. Frequencies of the single variables were compared by using the chi-squared test with Yates' correction. The correlation (r) was calculated by means of the Pearson correlation coefficient. The differences were considered significant when the P values were <0.05. The statistical analysis was done with the statistical program Solo-BMDPTM Statistical Software.

Results

In traffic policemen of male sex mean ACTH(P) levels were significantly higher than in control subjects (mean, SD P=0.040) (Table 1). The distribution of the ACTH(P) values in male traffic policemen and control subjects is significant and it is shown in Fig. 1. In traffic policemen of female sex mean ACTH(P) levels were significantly higher than in control subjects (mean, SD P=0.043) (Table 1). The distribution of the ACTH(P) values in female traffic policemen and control subjects is significant and it is shown in Fig. 2. Traffic policemen and control subjects with ACTH(P) values outside our laboratory's normal range were not included. In the present study we found little correlation (r=0.2) between ACTH(P) values and length of service in traffic policemen of male sex, and little correlation (r=0.2) was found between ACTH(P) values and length of service in traffic policemen of female sex.

Discussion

Considering that the principal confounding factors have been excluded and that the subjects investigated were matched by sex, age, length of service and drinking habit (<50 g of wine or beer per day), these data suggest the possibility that occupational exposure to urban pollutants and possible psycho-social stressors in traffic policemen could have an effect on ACTH(P) concentrations.

The fact that the differences between the means for exposed workers and controls are significant suggests that these differences may have clinical validity, even if the levels are within laboratory limits and the deviation is not as wide as is often seen in medical pathology. In fact, all the people included in or excluded from the study were asymptomatic and all the ACTH(P) values were within our laboratory's normal range (7.0–50 pg/m*l*).

The fact that there is little correlation (r) between ACTH(P) levels and length of service (r=0.2) for both traffic policemen and controls induces us to consider:

a) occupational exposure to stressors increases the ACTH(P) levels;

b) the ACTH(P) levels start increasing after a "brief" occupational exposure period and there is not a further increase or decrease after an increase in exposure.

The only study on human subjects, environmental pollutants and exposure time is about an acute intoxication by carbon monoxide[1].

The action mechanisms for the chemical substances able to influence the secretion of ACTH(P) are not yet clear. Studies on laboratory animals[3, 4] and on human subjects[1], have hypothesised that exposure to urban pollutants, could determine an increase (as for example in the case of benzene, toluene and carbon monoxide) or a diminution (mercury, cadmium, zinc and copper) of the neurohormone with both central and peripheral action[1–5].

Benzene and toluene possess both neurotoxic and immunotoxic effects; the ingestion of the two solvents could cause an increase in ACTH(P) in mice through the activation of the hypothalamic-pituitary-adrenal (HPA) axis[2]. It is well known that personal exposure to benzene, toluene and other aromatic hydrocarbons from direct exposure to traffic fumes, as experienced by some categories of outdoor workers, such as traffic policemen, may be considered higher than personal exposure of indoor workers (particularly in our cities)[35]. For this reason in our previous researches we have studied exposure dosage to benzene, toluene and other aromatic hydrocarbons in Municipal Police employees of the city in question. Time weighted average (TWA) exposure to benzene (mean 10.7 and 3.6 $\mu g/m^3$, respectively) and to toluene (mean 40.7 and 13.5 $\mu g/m^3$, respectively) was significantly higher among traffic policemen than among indoor workers[15–18]. Since previous studies have already measured the environmental and biological levels in our working population and it is well known that traffic policemen's exposure dosage is significantly higher than controls, we didn't repeat the exposure dosage study in this work.

An *in vitro* study on cells isolated from the rat adrenal cortex, have demonstrated that heavy metals (mercury, cadmium and copper) reduce the production of corticosteroid (CORT) stimulated by ACTH. The results indicated a direct toxic action of these heavy metals on steroid-producing cells in the adrenal gland[5].

In animal studies, acute administration of cadmium (Cd) causes a marked reduction in ACTH levels, whereas sub-chronic treatment causes an increase[3, 4].

In human subjects, acute carbon monoxide intoxication (CO) induces a marked increase in ACTH(P) levels, with values of 59 pg/m*l* in subjects with carboxyhemoglobin (COHb) <15% and 130 pg/m*l* in subjects with COHb>15%[1].

Aural stress has been observed to alter catecholamines, pituitary gland hormones and adrenal corticosteroids[6] both in animals and human subjects[6–8]. Animals exposed to 540 min of random noise per day for 8 d showed an increase in circulating ACTH levels[6]. A study on twelve paid male volunteers[8] exposed to industrial noise of 85 dB (A) from 09.00 to 21.00 h, showed temporarily increased levels of ACTH(P).

It has been demonstrated that psycho-social stressors alter ACTH(P) levels[13, 14]. It is well known that traffic policemen are a working population exposed to stress[36]. The constant attention required of traffic policemen in a noisy, polluted, badly lit and at times chaotic environment such as the street, requires constant application. Contact with the public, difficult conditions (illegality, tickets, arguments, accidents, injuries) certainly does not make the job easy or healthy. Therefore, stress for Municipal Police constables may be due to relations with citizens, exposure to criminal events or to the need to maintain high levels of performance in various contexts. In a previous study we analysed subjective stress in Municipal Police employees. To this end, we used the Rapid Stress Assessment scale (RSA): total RSA scores were found to be significantly higher in traffic policemen than in controls[37]. Moreover the HPA axis activation with an ACTH(P) increase due to stressors could be associated with clinical depression according to several studies[10–12].

Conclusion

It can be supposed that urban pollution can interact with psycho-social stressors and that both chemical and physical agents and psycho-social agents can alter the neuroendocrine system[38].

The results obtained through our research support the hypothesis that traffic policemen exposed to the abovementioned stressors, present in this city, can have an increase in ACTH(P) concentrations.

It can therefore be supposed that the increase in ACTH(P) concentrations could be a useful early biological marker of exposure to pollutant substances, usable in occupational settings. Such changes might be regarded as early signs of risk for the general population exposed to environmental stressors also, even if ways and times are different from those of working populations.

References

1) H Raff, RW Goldmann and EP Kindwall: Adrenocortical function after acute carbon monoxide exposure in humans. Arch Environ Health 40, 88–90 (1985)
2) GC Hsieh, RP Sharma and RD Parker: Hypothalamic-pituitary-adrenocortical axis activity and immune function after oral exposure to benzene and toluene. Immunopharmacology 21, 23–31 (1991)
3) A Lafuente and AI Esquifino: Modulation of episodic adrenocorticotropin hormone secretion by cadmium in male rats. Biometals 11, 183–188 (1998)
4) A Lafuente and AI Esquifino; Cadmium effects on hypothalamic activity and pituitary hormone secretion in the male. Toxicol Lett 110, 209–218 (1999)
5) TB Ng and WK Liu: Toxic effect of heavy metals on cells isolated from the rat adrenal and testis. In Vitro

Cell Dev Biol Anim 26, 24–28 (1990)
6) MT Van Raaij, CJ Dobbe, B Elvers, A Timmerman, E Schenk, M Oortigiesen and VM Wiegant: Hormonal status and the neuroedocrine response to a novel heterotypic stressor involving subchronic noise exposure. Neuroendocrinology 65, 200–209 (1997)
7) B Fruhstorfer, H Fruhstorfer, P Grass, HG Milerski, G Sturm, W Wesemann and D Wiesel: Daytime noise stress and subsequent night sleep: interference with sleep patterns, endocrine and neurocrine functions. Int J Neurosci 26, 301–310 (1985)
8) B Fruhstorfer, MG Pritsch, P Ott and G Sturm: Effects of daytime noise load on the sleep-wake cycle and endocrine patterns in man: II. 24 hours secretion of anterior and posterior pituitary hormones and of cortisol. Int J Neurosci 39, 211–221 (1988)
9) J Stejskal and VD Stejskal: The role of metals in autoimmunity and the link to neuroendocrinology. Neuroendocrinology Letters 20, 351–364 (1999)
10) I Heuser, M Deuschle, P Luppa, U Schweiger, H Standhardt and B Weber: Increased diurnal plasma concentration of dehydroepiandrosterone in depressed patients. J Clin Endocrinol Metab 83, 3130–3133 (1998)
11) ML Wong, MA Kling, PJ Munson, S Listwak, J Licinio, P Prolo, B Karp, JE McCutcheon, TD Jr Geracioti, MD DeBellis, KC Rice, DS Goldstein, JD Veldhuis, GP Chrousos, EH Oldfield, SM McCann and PW Gold: Pronounced and sustained central hypernoradrenergic function in major depression with melancholic features: relation to hypercotisolism and corticotropin-releasing hormone. Proc Natl Acad Sci USA 97, 325–330 (2000)
12) R Galard, R Catalan, JM Castellanos and JM Gallart: Plasma corticotropin-releasing factor in depressed patients before and after the dexamethasone suppression test. Biol Psychiatry 51, 463–468 (2002)
13) G Gerra, A Zaimovic, GG Mascetti, S Gardini, U Zambelli, M Timpano, MA Raggi and F Brambilla: Neuroendocrine responses to experimentally-induced psychological stress in healthy humans. Psychoneuroendocrinology 26, 91–107 (2001)
14) A Singh, JS Petrides, PW Gold, GP Chrousos and PA Deuster: Differential hypothalamic-pituitary-adrenal axis reactivity to psychological and physical stress. J Clin Endocrinol Metab 84, 1944–1948 (1999)
15) F Tomei, S Ghittori, M Imbriani, S Pavanello, A Carere, F Marcon, A Martini, TP Baccolo, E Tomao, A Zijno and R Crebelli: Environmental and biological monitoring of traffic wardens from the city of Rome. Occup Med (Lond) 51, 198–203 (2001)
16) R Crebelli, F Tomei, A Zijno, S Ghittori, M Imbriani, D Gamberale, A Martini and A Carere: Exposure to benzene in urban workers: environmental and biological monitoring of traffic police in Rome. Occup Environ Med 58, 165–171 (2001)
17) A Verdina, R Galati, G Falasca, S Ghittori, M Imbriani, F Tomei, L Marcellini, A Zijno, V Del Vecchio and R Crebelli: Metabolic polymorphisms and urinary biomarkers in subjects with low benzene exposure. J Toxicol Environ Health (A) 64, 607–618 (2001)
18) R Galati, A Zijno, R Crebelli, G Falasca, F Tomei, F Iecher, P Carta and A Verdina: Detection of antibodies to the benzo(a)pyrene diol epoxide-DNA adducts in sera from individuals exposed to low doses of polycyclic aromatic hydrocarbons. J Exp Clin Cancer Res 20, 359–364 (2001)
19) C Kirschbaum, BM Kudielka, J Gaab, NC Schommer and DH Hellhammer: Impact of gender, menstrual cycle phase, and oral contraceptives on the activity of the hypothalamus-pituitary-adrenal axis. Psychosom Med 61, 154–162 (1999)
20) F Cucinelli, L Soranna, A Barini, C Perri, F Leoni, S Mancuso and A Lanzone: Estrogen treatment and body fat distribution are involved in corticotropin and cortisol response to corticotropin-releasing hormone in postmenopausal women. Metabolism 51, 137–143 (2002)
21) EA Young, M Altemus, V Parkison and S Shastry: Effects of estrogen antagonists and agonists on the ACTH response to restraint stress in female rats. Neuropsychopharmacology 25, 881–891 (2001)
22) D Spassova, T White and AK Singh: Acute effects of acephate and methamidophos on acetylcholinesterase activity, endocrine system and amino acid concentrations in rats. Comp Biochem Physiol C Toxicol Pharmacol 126, 79–89 (2000)
23) TE Stoker, JM Goldman, RL Cooper and WK McElroy: Influence of chlordimeform on alpha-adrenergic receptor-associated mechanisms of hormonal regulation in the rat: pituitary and adrenocortical secretion. Toxicology 69, 257–268 (1991)
24) HG Ortega, M Lopez, A Takaki, QH Huang, A Arimura and JE Salvaggio: Neuroimmunological effects of exposure to methylmercury forms in the Sprague-Dawley rats. Activation of the hypothalamic-pituitary-adrenal axis and lymphocyte responsiveness. Toxicol Ind Health 13, 57–66 (1997)
25) V Coiro and PP Vescovi: Effect of cigarette smoking on ACTH/cortisol secretion in alcoholics after short- and medium term abstinence. Alcohol Clin Exp Res 23, 1515–1518 (1999)
26) C Waltman, LS Jr Blevins, G Boyd and Gs Wand: The effects of mild ethanol intoxication on the hypothalamic-pituitary-adrenal axis in nonalcoholic men. J Clin Endocrinol Metab 77, 518–522 (1993)
27) Lukas SE and Mendelson JH: Electroencephalographic activity and plasma ACTH during ethanol-induced euphoria. Biol Psychiatry 23, 141–148 (1988)
28) X Dai, J Thavundayil and C Gianoulakis: Response of the hypothalamic-pituitary-adrenal axis to stress in the absence and presence of ethanol in subjects at high and low risk of alcoholism. Neuropsychopharmacology 27, 442–452 (2002)
29) S Lee, ED Schmidt, FJ Tilders and C Rivier: Effect of repeated exposure to alcohol on the response of the hypothalamic-pituitary-adrenal axis of the rat: I. Role of changes in hypothalamic neuronal activity. Alcohol Clin Exp Res 25, 98–105 (2001)
30) C Rivier, T Imaki and W Vale: Prolonged exposure to alcohol: effect on CRF mRNA levels, and CRF-and

stress-induced ACTH secretion in the rat. Brain Res 520, 1–5 (1990)
31) K Ogilvie, S Lee and C Rivier: Effect of three different modes of alcohol administration on the activity of the rat hypothalamic-pituitary-adrenal axis. Alcohol Clin Exp Res 21, 467–476 (1997)
32) J Frias, JM Torres, MT Miranda, E Ruiz and E Ortega: Effects of acute alcohol intoxication on pituitary-gonadal axis hormones, pituitary-adrenal axis hormones, beta-endorphin and prolactin in human adults of both sexes. Alcohol Alcohol 37, 169–173 (2002)
33) G Kertesz, B Bourcier, H Cailla and F Jean: Immunoradiometric assay of succinylated corticotropin: an improved method for quantification of ACTH. Clin Chem 44, 78–85 (1998)
34) S Gibson, A Pollock, M Littley, S Shalet and A White: Advantages of IRMA over RIA in the measurement of ACTH. Ann Clin Biochem 26, 500–507 (1989)
35) S Fustinoni, M Buratti, R Giampiccolo and A Colombi: Biological and environmental monitoring of exposure to airborne benzene and other aromatic hydrocarbons in Milan traffic wardens. Toxicol Lett 77, 387–392 (1995)
36) MD Piercecchi-Marti, G Leonetti, AL Pelissier, J Conrath, F Cianfarani and M Valli: Evaluation of biological stress markers in police officers. Med Law 18, 125–144 (1999)
37) P Pancheri, A Martini, L Tarsitani, MV Rosati, M Biondi and F Tomei: Assessment of subjective stress in the Municipal Police Force of the city of Rome. Stress and Health 18, 127–132 (2002)
38) F Tomei, B Papaleo, TP Baccolo, B Persechino, G Spanò and MV Rosati: Noise and gastric secretion. Am J Ind Med 26, 367–372 (1994)