

Color Vision Impairment in Workers Exposed to Neurotoxic Chemicals

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Abstract

Recent research shows that occupational exposure to several solvents, metals and other industrial chemicals can impair color vision in exposed workers. Occupation-related color vision impairment usually results in blue–yellow color discrimination loss or, less frequently, a combination of blue–yellow and red–green loss. The eyes may be unequally involved, and the course is variable depending on exposure and other factors. The pathogenesis of occupational color vision loss has not been elucidated; it may be due to, e.g. a direct action of neurotoxins on receptors, possibly on the cone's membrane metabolism, and/or to an interference with neurotransmitters within the retina. Other possible pathogenetic mechanisms, such as a direct effect to the optic nerve, have also been suggested. Occupational color vision loss is usually sub-clinical, and workers are unaware of any deficit. It can be assessed using sensitive tests, such as the Farnsworth–Munsell 100 Hue (FM-100) or the Lanthony D-15 desaturated panel (D-15 d). The latter is the most widely used for studies in groups of exposed workers, and offers the possibility of a quantitative evaluation of the results by calculation of the Bowman's Color Confusion Index (CCI), or of the Vingrys' and King Smith's Confusion Index (CI). Other advantages of D-15 d are the possibility to perform the test directly at the workplace, and the reproducibility when performed in standardized conditions. In most cases, occupation-related color vision impairment is correlated to exposure levels, and has often been observed in workers exposed to environmental concentrations below the current occupational limit proposed by the ACGIH. Progression with increasing cumulative exposure has been reported, while reversibility is still discussed. Acquired color vision impairment related to occupational exposure to styrene, perchloroethylene (PCE), toluene, carbon disulfide, n-hexane, solvent mixtures, mercury and some other chemicals are discussed. Results show that color vision testing should be included in the evaluation of early neurotoxicity of chemicals in exposed workers. The D-15 d would be useful in the surveillance of workers exposed to solvents and other chemicals toxic to the visual system.

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INTRODUCTION

Researchers have only recently addressed the topic of color perception in workers occupationally exposed to chemicals and very few studies were published before the late eighties. The increasing interest in recent years has resulted in the progressive discovery

of a previously unknown effect of occupational exposure: color-perception impairment.

Occupation-related color vision impairment, like other acquired dyschromatopsias, usually results in an impairment of blue–yellow color discrimination or, less frequently, in a combination of blue–yellow and red–green loss, while congenital dyschromatopsias more frequently result in red–green deficits (Verriest, 1963; Hart, 1987, 1992; Mergler et al., 1987). Furthermore, in acquired dyschromatopsia the impairment can involve the eyes unequally or be monocular, and

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can have a variable, progressive or regressive course, depending on various factors, including exposure (Verriest, 1963; Dubois-Poulsen, 1972; Pokorny et al., 1979; Mergler et al., 1987; Hart, 1992; Gobba and Cavalleri, 2000).

The possible pathogenesis of color vision loss in chemical exposed workers is unclear. According to the so-called “Kollner’s rule”, the finding that the blue–yellow range of color vision is usually affected suggests a retinal location of the effect (Hart, 1987). This is in agreement with some electrophysiological data obtained in workers exposed to styrene and PCE (Mirzoev and Sultanov, 1989) and in experimental exposure of animals to various solvents (Carricaburu et al., 1980). A possible mechanism may be related to a direct effect of the chemicals, or active metabolites, on cone functioning, and/or to an interference with neurotransmitters, like dopamine. Alternatively, color vision loss may be the result of a distal (dying back) axonopathy of the optic pathway, as suggested by Schaumburg and Spencer (1978) for *n*-hexane. Nevertheless, pathogenic mechanisms require further research.

Recent results from Dick et al. (2000) suggest that color vision loss may be part of a neurological syndrome related to organic solvents exposure, also including coarse tremor, impaired vibration sensation in the legs and cognitive impairment; nevertheless these results deserve to be confirmed in further studies.

METHODS FOR COLOR VISION TESTING IN GROUPS OF WORKERS

Several methods can be applied for color vision testing (Hart, 1987). The most widely used are the pseudo-isochromatic plates, as the Ishihara tables, designed to evaluate congenital color vision loss in the red–green range. However, these tests are not adequate for the early detection of acquired dyschromatopsias (Verriest, 1964; Pokorny et al., 1979). Another category of tests include color arrangement, or hue discrimination tests. The best known is probably the Farnsworth–Munsell 100 Hue (FM-100), that is based on the ability to recombine the chromatic sequence formed by a set of 85 caps separated into four groups. The FM-100 provides a highly sensitive quantitative measure of color vision defects, including both congenital and acquired dyschromatopsias (Hart, 1987, 1992). However, this test is quite time-consuming, and has seldom been applied in studies “in the field” on groups of workers. The test most commonly used in the occupational setting is the Lanthony D-15 desaturated panel (D-15 d), composed of a single set of

15 caps with desaturated colors (Lanthony, 1978). This test can be considered a kind of “shorter version” of the FM-100, whose sensitivity has been increased by the use of desaturated colors. The D-15 d is used in studies on groups of exposed workers as it is sensitive enough for the early detection of mild acquired dyschromatopsia (Mergler et al., 1987), and it is much less time-consuming than the FM-100 (it usually takes only a few minutes). Furthermore, it is simple and well accepted by workers and can be easily carried out directly in the workplace.

In performing D-15 d it is important to use standardized conditions (Geller and Hudnell, 1997). Each eye must be tested separately, as acquired-impairment in color vision may be monocular or asymmetrical (Hart, 1992). We currently apply the D-15 d in the morning, before exposure, using a daylight fluorescent lamp (color temperature 5000 K) providing 1200 lx on the work plane, since results obtained using different lighting conditions are not comparable (D’Zmura et al., 1998).

A problem in the evaluation of the results of D-15 d testing in exposed workers is that accepted reference limits are not available, and consequently a comparison with adequate referents is needed. We usually select a control group matched for sex, age (± 5 years), tobacco smoking (± 10 cigarettes per day), and alcohol consumption (± 10 g per day). Recently, some authors have proposed statistical methods to adjust results for age and alcohol consumption (e.g. Campagna et al., 1995; Zavalic et al., 1998a,b).

An important aspect in the studies on occupation-related color vision impairment is that the sensitivity of D-15 d testing may be inadequate to disclose early color vision impairment, if the results are only qualitatively evaluated.

One of the key features of the D-15 d that has led to its use in studies in occupational medicine, is the possibility to quantitatively express the outcomes, greatly improving the comparison of the results between exposed workers and referents, and enabling the study of dose–effect relationships. For quantitative scoring of D-15 d, the methods proposed by Bowman (1982) or by Vingrys and King-Smith (1988) can be applied. The former method is the most frequently applied in studies published to date, and gives the procedure to calculate a “score”, and also to calculate the Color Confusion Index (CCI). The CCI value is 1 when the test is completed correctly by the subject, while each error in recombining the correct sequence of the caps increases this value. The higher the number and relevance of errors, the higher the CCI. The other

Table 1
Main industrial solvents, and industrial metals and other chemicals inducing color vision loss in exposed workers

Main industrial solvents	
Styrene	Gobba et al. (1991, 1993), Fallas et al. (1992), Chia et al. (1994), Campagna et al. (1995, 1996), Eguchi et al. (1995), Mergler et al. (1996), Castillo et al. (2001), Kishi et al. (2001), Triebig et al. (2001)
Perchloroethylene	Alieva et al. (1985), Nakatsuka et al. (1992), Gobba et al. (1993), Cavalleri et al. (1994), Gobba et al. (1998)
Toluene	Bælum et al. (1985, 1990), Nakatsuka et al. (1992), Muttray et al. (1995, 1999), Zavalic et al. (1996, 1998a,b), Cavalleri et al. (2000), Campagna et al. (2001)
Carbon disulfide	Raitta et al. (1981), Ruijiten et al. (1990), Vanhoorne et al. (1996)
<i>n</i> -Hexane	Raitta et al. (1978), Nylén et al. (1993)
Solvent mixtures	Blain et al. (1985), Mergler and Blain (1987), Mergler et al. (1987, 1988, 1991), Baird et al. (1994), Broadwell et al. (1995), Zdieszynska and Gos (1995), Zavalic et al. (1996), Muttray et al. (1997), Valic et al. (1997), Gonzalez et al. (1998), Gobba et al. (1999), Dick et al. (2000), Semple et al. (2000), Till et al. (2001, 2002)
Main industrial metals and other chemicals	
Mercury	Cavalleri et al. (1995), Cavalleri and Gobba (1998), Gobba et al. (1996), Urban et al. (2002)
Organophosphate pesticides	Dick et al. (2001)
2- <i>t</i> -Butylazo-2-hydroxy-5-methylxane	Horan et al. (1985)

method (Vingrys and King-Smith, 1988) explains how to calculate three indices: the Confusion Index (C index), giving the degree of error relative to a perfect score, the Confusion Angle, indicating the type of defect, and the Scatter Index, measuring the polarity, or symmetry, of the impairment. Even if less used so far, the indices proposed by Vingrys and King-Smith (1988) do offer some advantages in terms of characterization of the D-15 d outcomes. Furthermore, according to our preliminary results, the C index seems more sensitive than Bowman's CCI in highlighting early color vision deficit in solvent-exposed workers, as we have observed in toluene workers: significance in difference between exposed and controls, and correlation coefficients with exposure resulted higher using the Vingrys and King-Smith's C index (Cavalleri et al., 2000).

Applying the D-15 and/or, less frequently, other methods, impairment in color vision has been observed in workers exposed to several solvents, solvent mixtures and metals. The main findings are summarized in Table 1. A general review of current knowledge is the objective of this paper.

MAIN INDUSTRIAL SOLVENTS ASSOCIATED TO ACQUIRED COLOR VISION IMPAIRMENT IN EXPOSED WORKERS

Styrene

Styrene was one of the first solvents investigated by our group in 1991, and it is one of the most studied

compounds. We observed an impairment in color vision in a group workers exposed to this solvent during the production of Fiberglass-Reinforced Plastics (FRP) (Gobba et al., 1991). The effect was significantly correlated to the Time Weighted Average (TWA) exposure level obtained by personal sampling (Fig. 1). Later, we confirmed the observation in further groups of styrene exposed workers (Gobba and Cavalleri, 1993). Similar data were also reported by other groups (Fallas et al., 1992; Chia et al., 1994; Campagna et al., 1995, 1996; Eguchi et al., 1995; Kishi et al., 2001), confirming that styrene can induce an impairment in color vision and that this effect is dose related (Chia et al., 1994; Campagna et al., 1995, 1996; Eguchi et al., 1995).

Interestingly, from a comparison of published results we realized that, when the Lanthony D-15 d was performed in standardized conditions, the results independently obtained by different groups were very similar. As an example, the results of correlation between exposure (Time Weighted Average airborne styrene levels) and CCI obtained in Italy in our first study (Gobba et al., 1991) and in Canada by Campagna et al. (1995) were virtually identical. This was very important as it confirmed both the effect of styrene on color vision and the reproducibility of the D-15 d. We decided to pool our data with the data obtained by Campagna et al. (1995) to investigate a possible threshold for styrene induced effect on color vision (Campagna et al., 1996). The results showed that an impairment could be significantly detected at environmental levels of styrene as low as 4 ppm (17 mg/m³) (Campagna et al., 1996).

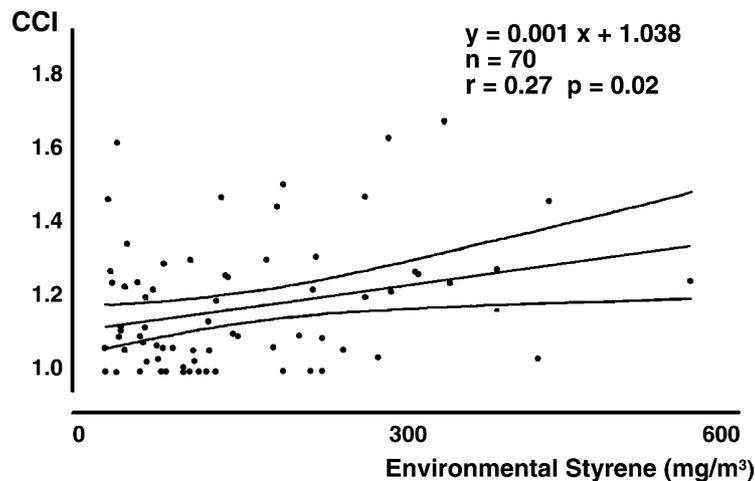


Fig. 1. Correlation, and 95% confidence interval for the predicted mean values of the dependent variable, between Time Weighted Average (TWA) environmental concentrations of styrene measured by personal passive sampling and values of the Color Confusion Index (CCI) in 70 exposed workers.

The analysis of the results of our studies led us to another observation. It is known that color discrimination decreases with age and, as an example, regression lines between age and CCI were proposed by Bowman et al. (1984), and our group (Gobba and Cavalleri, 2000). Knowledge on factors behind this effect of aging is far from complete: age-related changes in the ocular media and in the retina are well documented, but compensation mechanisms also occur (Werner, 1996; Knoblauch et al., 2001). A discussion of these aspects of vision is complex, and it is beyond the objectives of this review. Nevertheless, in a group of styrene exposed workers we observed that, apparently, this solvent seems to have a synergistic effect with age-related color vision loss (Gobba et al., 1991). An effect on the retina may be assumed, but adequate studies to support this hypothesis are lacking.

To date, only few studies have evaluated the time course of styrene-related color-perception impairment, and the results are conflicting.

To study short-term course, we examined 41 exposed workers during the last week of work before the summer holidays, and on the morning of the first working day after vacation, before exposure. Mean CCI values measured before and after the holidays were not significantly different, suggesting that an interruption in exposure lasting 30 days cannot reduce styrene-related color vision loss. Different results were recently presented by Triebig et al. (2001), who observed a complete recovery of styrene-related CCI impairment in 22 FRP workers after a 4 weeks vacation. The reasons for the discrepancy in results between these two studies are not clear. However, there are

some differences: Triebig et al. (2001) excluded the results of more than 27% of exposed workers, and 43% of controls, and applied the Lanthony D-15 binocularly. Furthermore, styrene exposure was lower, and exposure duration shorter compared to our study (Gobba et al., 1991).

Regarding the course in longer periods, Mergler et al. (1996) studied a group of styrene exposed workers over a 2-year period. A dose–response progression or regression of the effect was observed depending on whether exposure increased or decreased. In a group of 30 FRP workers (Gobba and Cavalleri, 2000), we studied exposure and color vision, and a new survey was carried out 12 months later. Exposure had increased in 10 workers, even if the difference was not significant, while styrene levels were unchanged or slightly reduced in the other 20. In the group where exposure had increased, a progression towards worsening in color vision loss was observed, while mean CCI values remained unchanged in workers with the same exposure. In another study conducted in 18 FRP workers, a reduction in exposure did not result in any significant improvement (Castillo et al., 2001).

Accordingly, available data suggest a progression of styrene-related color-perception loss during 1–2 years periods when exposure is increased (Mergler et al., 1996; Gobba and Cavalleri, 2000). Regarding reversibility results are conflicting. A 1 month interruption in exposure seems to have no effect on color vision impairment (but different results have been published), while a reduction in exposure lasting longer periods (1 year or more) resulted in a regression or had no effect. This topic certainly deserves further development.

Perchloroethylene (PCE)

Another solvent that can impair color vision at low exposure levels is perchloroethylene (PCE). We studied the effect of this solvent in a group of dry-cleaners exposed to a mean TWA environmental concentration of PCE of 7 ppm (Gobba et al., 1993; Cavalleri et al., 1994). This exposure level is about 30% of the current limit proposed by ACGIH (ACGIH, 2000). Color vision among exposed workers was significantly worse than that of matched referents. Furthermore, CCI values proved significantly correlated to PCE environmental concentrations (Fig. 2) ($r = 0.52$; $P < 0.01$), indicating that for PCE the effect is also dose-related (Cavalleri et al., 1994), as is the case of styrene. These results were confirmed in another independent group of dry-cleaners (Gobba et al., 1997).

There are only a few other studies on color vision effect of PCE. Alieva et al. (1985) published, in Russian, a paper describing a high prevalence of dyschromatopsias in a group of workers exposed to high levels of the solvent. Comparisons to the results of this study are difficult, since the description of the methods and results is sketchy. Furthermore, environmental levels of the solvent were so high as to induce subjective symptoms like lacrimation and conjunctivitis, and the described color vision damage involved the red–green range.

In another study, Nakatsuka et al. (1992) failed to find any color vision impairment in workers exposed to about 50% of the current TLV–TWA (ACGIH, 2000). This author used the Lanthony's new color test and the Ishihara's color vision test. These tests differ from the

Lanthony D-15 in various aspects (for a review on this topic see Geller and Hudnell, 1997; Iregren et al., 2002a,b) and are less sensitive for detection of early acquired color vision loss (Mergler et al., 1987). Furthermore, the outcomes were not evaluated using an adequate quantitative method similar to the CCI (Bowman, 1982), or the Confusion Index (Vingrys and King-Smith, 1988). Lastly in Nakatsuka et al.'s (1992) study, the exclusion criteria were not reported, and exposed subjects and referents were not matched for parameters like age, alcohol consumption and cigarette smoking. Accordingly, we do not think that if their results are comparable with previous data (Gobba et al., 1993; Cavalleri et al., 1994).

The development of color vision loss was also studied in PCE exposure (Gobba et al., 1998). In a group of 33 dry-cleaners, exposure was evaluated by personal passive sampling, and color perception tested using the D-15 d. Airborne TWA levels of PCE were lower than the TLV proposed by ACGIH (ACGIH, 2000): the geometric mean was 2.4 ppm. An increase in CCI was observed compared to a group of matched referents. Mean values were 1.16 (0.14; S.D.) versus 1.02 (0.08; S.D.), respectively, $P < 0.05$. The same workers were re-examined 24 months later. Environmental monitoring results showed an increase in exposure in 19 workers and a reduction in the remaining 14. In the first group (exposure increased), color vision had significantly worsened, while in the remaining 14 subjects no variation in CCI values was observed. These data suggest that also for PCE occupational-related color vision loss may worsen as exposure increases, but, apparently, is not reversed by a (slight)

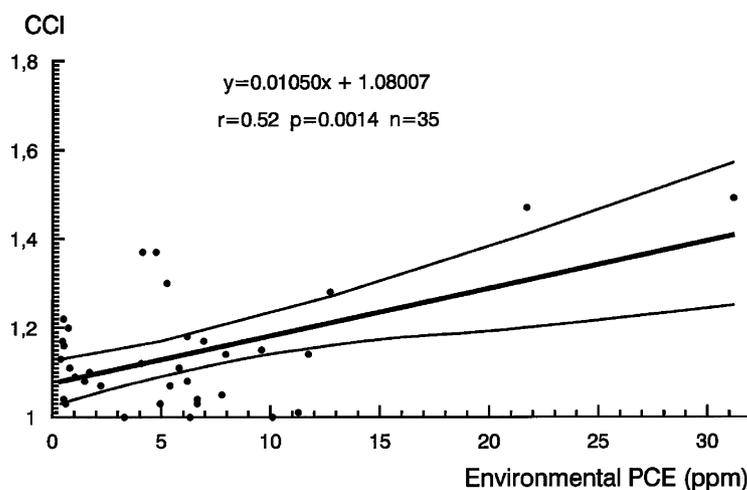


Fig. 2. Correlation, and 95% confidence interval for the predicted mean values of the dependent variable, between Time Weighted Average (TWA) environmental concentrations of perchloroethylene measured by personal passive sampling and values of the Color Confusion Index (CCI) in 35 exposed workers (from Cavalleri et al., 1994).

reduction of exposure level. Nevertheless, the effect of a reduction in exposure is not clear, and further studies on this topic are needed.

Toluene

The effect of toluene on color perception was studied by several researchers (Bælum et al., 1985, 1990; Nakatsuka et al., 1992; Muttray et al., 1995, 1999; Zavalic et al., 1998a,b; Cavalleri et al., 2000; Campagna et al., 2001).

An acute experimental exposure to 100 ppm of toluene lasting 6.5 h induced a decrease in color discrimination in a group of 43 workers compared to 43 controls (Bælum et al., 1985), but the results were not confirmed (Bælum et al., 1990). No effect was observed following 30 min exposure to about 300 ppm of toluene in a small group of rotogravure print-shop workers (Muttray et al., 1999). In another study, the same solvent did not induce any significant sub-acute adverse effect on color vision in exposed workers (Muttray et al., 1995).

On the other hand, impairment in color discrimination has been observed in workers chronically exposed to toluene. Recently, Zavalic et al. (1998a,b) reported a significant impairment in workers exposed to TWA median levels of toluene of 132 ppm, but not in another group exposed to 32 ppm. Nevertheless, in these studies confounders as gender and alcohol consumption were not adequately evaluated.

Recently we studied 33 rubber workers exposed to an estimated level of the solvent of 42 ppm, that is lower than the occupational limit for toluene (50 ppm)

proposed in USA by ACGIH (ACGIH, 2000), and in Germany (Deutsche BAT, 1990). Color vision proved significantly impaired in exposed compared to matched controls (Cavalleri et al., 2000).

The results suggest that chronic exposures ranging around the current occupational limits can significantly affect color perception.

Different results were reported by Nakatsuka et al. (1992), who failed to observe any color vision loss in subjects exposed to mean concentrations of toluene of 44 ppm. The limitations of the method applied by these authors have been discussed above, in section “Perchloroethylene (PCE)”. The lack of effect in Nakatsuka’s study is likely to be due to the protocol applied.

Data on the development of color vision loss in toluene exposed workers are lacking, but we found that the reduction in color perception, evaluated by CCI, was significantly related to an index representative of the total “cumulative” exposure to the solvent (CumExp), calculated as follows: $\text{CumExp} = \text{TolU} (\mu\text{g/l}) \times \text{exposure duration (months)}$ (Fig. 3) (Cavalleri et al., 2000). Recently, Campagna et al. (2001) also reported a positive relationship between color vision loss and cumulative toluene exposure.

Other Solvents

A possible effect on color perception has been evaluated also in carbon disulfide and *n*-hexane exposure. Using the Farnsworth–Munsell 100 Hue test, Raitta et al. (1981) and, more recently, Vanhoorne et al. (1996) observed a sub-clinical impairment in carbon disulfide exposed workers. Data on dose–effect

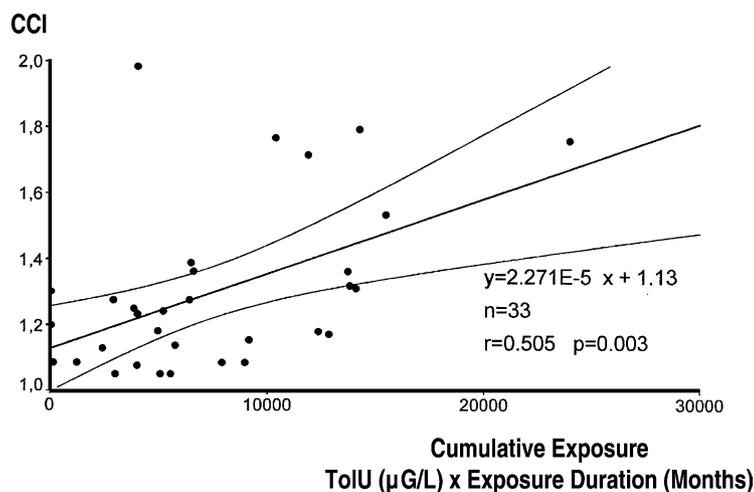


Fig. 3. Correlation, and 95% confidence interval for the predicted mean values of the dependent variable, between cumulative exposure to toluene ($\text{CumExp} = \text{TolU} (\mu\text{g/l}) \times \text{exposure duration (months)}$) and values of the Color Confusion Index (CCI) in 33 exposed workers. TolU = urinary toluene in end-shift samples. (from Cavalleri et al., 2000).

relation are insufficient but, according to Vanhoorne et al.'s (1996) results, the current TLV–TWA for CS₂ (10 ppm) seems protective enough against this effect. This conclusion is in agreement with the results obtained by Ruijiten et al. (1990) using the D-15 d.

Only few data are available on the effect on color perception of occupational exposure to *n*-hexane. Color vision defects, mainly in the blue–yellow spectrum, were observed in workers exposed to presumably high environmental levels of this solvent, but the study did not include a control group (Raitta et al., 1978). Experimental data on animals clearly support the hypothesis that simultaneous co-exposure to intense light can act as a synergistic factor on hexane induced ocular toxicity (Nylén et al., 1993).

Solvent Mixtures

Several authors have studied the effect of occupational exposure to solvent mixtures on color vision (Blain et al., 1985; Mergler and Blain, 1987; Mergler et al., 1987, 1988, 1991; Baird et al., 1994; Zdziszynska and Gos, 1995; Zavalic et al., 1996; Muttray et al., 1997; Valic et al., 1997; Gonzalez et al., 1998; Gobba et al., 1999; Dick et al., 2000; Semple et al., 2000). The main problem in the comparison of these studies is that the term “solvent mixtures” mostly is too vague. A large number of solvents are generally included in mixtures, with different toxicokinetics and effects, and metabolic and toxic interactions are likely. A suggestion for future studies is to introduce a more precise characterization of mixtures, e.g. based on measure of the main components. This would be of great help in comparing the results reported by different authors.

In spite of these limitations, most of the studies are in agreement in showing an impairment in color vision in exposed workers. A study of the relation between exposure levels and effect is however hindered by the reasons previously reported on the various solvents included in different mixtures. Still, in a few studies (Muttray et al., 1997; Gobba et al., 1999) the total solvent load was calculated according to the method proposed for mixtures by the ACGIH (2000), and the results reported suggest a possible threshold at environmental levels much lower than that obtained by using the ACGIH proposed limits (ACGIH, 2000).

In contrast to these findings, at least three published papers failed to detect color vision loss in workers exposed to solvent mixtures (Nakatsuka et al., 1992; Baird et al., 1994; Broadwell et al., 1995). In the study

by Baird et al. (1994) solvent exposure was very low, in the order of 6% of the ACGIH TLV (Mergler, 1995). It is also not clear if color vision testing was done monocularly or binocularly, and the results obtained in exposed workers were not compared to a non-exposed control group. In the second paper (Broadwell et al., 1995), an unusually high prevalence of dyschromatopsia was observed in controls. The observations on the protocol applied in the third negative study, by Nakatsuka et al. (1992), are presented in sections “Styrene” and “Perchloroethylene (PCE)”.

Another aspect of solvent toxicity to visual functions, almost completely unknown to date, is the possible association between occupational exposure to organic solvents during pregnancy and increased risk of color vision impairment (and also of poorer visual acuity) in offspring (Till et al., 2001, 2002). The impact of gestational exposure to solvents on the developing visual system has received little attention, but the results of Till et al. (2001, 2002) are disturbing, and deserve appropriate attention. Moreover, they further support the need to avoid exposure to organic solvents during pregnancy.

MAIN METALS AND OTHER CHEMICALS ASSOCIATED TO ACQUIRED COLOR VISION IMPAIRMENT IN EXPOSED WORKERS

Even if various metals as lead, manganese or gallium can affect vision (Csaky and Caruso, 1997; Gobba, 2000), only little effort has been made to study the effect of occupational exposure to metals on color vision to date. Studies on color perception in groups of workers were performed only for mercury exposure.

Mercury

We studied the effects of metallic mercury in a group of workers exposed during the production of precision instruments (Cavalleri et al., 1995). Biological monitoring results showed a high exposure: mean urinary Hg excretion (HgU) was 114 µg/g creatinine, and all workers but one exceeded the current Biological Exposure Index (BEI) proposed by ACGIH (35 µg/g creatinine) (ACGIH, 1997). Color discrimination testing revealed a dose-related impairment, and the data are presented in Fig. 4 (Cavalleri et al., 1995). These results have been confirmed in a study of Urban et al. (2002), also suggesting a threshold for the effect at HgU levels below the current BEI proposed by ACGIH (ACGIH, 2000).

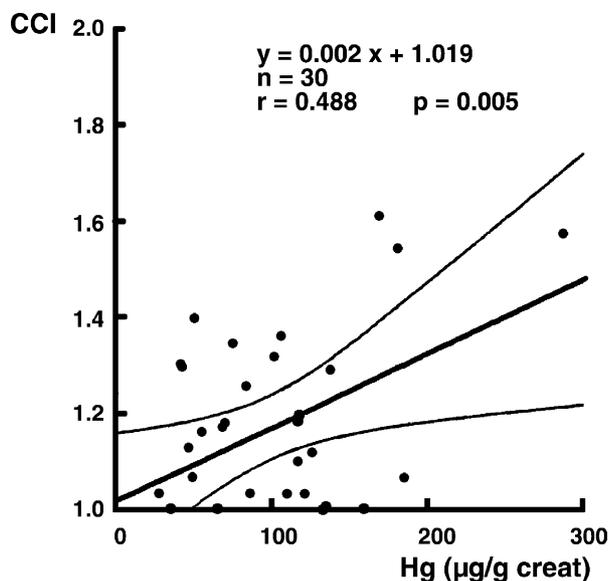


Fig. 4. Correlation, and 95% confidence interval for the predicted mean values of the dependent variable, between urinary Hg in pre-shift samples and values of the Color Confusion Index (CCI) in 30 exposed workers (from Cavalleri et al., 1995).

In the group of workers studied in 1995 (Cavalleri et al., 1995), we were able to follow the development of color vision loss. Indeed, as a result of our survey, working conditions were improved to reduce exposure. Twelve months later, biological monitoring and color vision testing were repeated in 21 of the workers examined during the first survey (Gobba et al., 1996; Cavalleri and Gobba, 1998). The urinary excretion of the metal was less than 1/10 compared to the previous survey: mean HgU was 10.0 µg/g versus 114 µg/g creatinine, and in no worker was the BEI limit exceeded. Color vision test results showed a significant improvement of mean CCI compared to the first survey (1.28 versus 1.12; $P < 0.01$). In addition, any difference compared to referents' had disappeared, indicating an almost complete regression of the impairment.

Other Chemicals

Impairment of color vision was reported in workers exposed to other chemicals as organophosphate compounds (Dick et al., 2001), or 2-*t*-butylazo-2-hydroxy-5-methylxane (Horan et al., 1985), but published studies are certainly few.

CONCLUSIONS

Although a relatively small number of industrial chemicals has been studied until now, the data presented

here show that occupational exposure to several solvents, and at least to one metal, mercury, can induce a color vision loss in workers. The results of these studies strongly suggest that color vision testing should be part of research into the early neurotoxicity of chemicals.

Chemical related color vision loss is usually sub-clinical, but development into clinically overt dyschromatopsia cannot be ruled out, and the results of some studies suggesting a correlation between impairment and cumulative exposure are in agreement with this hypothesis. Furthermore, there is no doubt that the reduction in color vision is related to ocular/retinal toxicity of the chemical, and this is certainly of primary concern. Accordingly, follow-up studies in workers exposed to ophthalmotoxic chemicals are needed to evaluate the development of this visual impairment.

For various solvents, and also for mercury, a significant effect can be observed in workers exposed to environmental levels lower than the occupational limits proposed, e.g. by ACGIH, or by the Deutsche Forschungsgemeinschaft, suggesting the need for a careful re-evaluation of these limits, considering the effect on visual perception.

Finally, color vision testing using the Lanthony D-15 desaturated panel would be useful in the surveillance of workers exposed to solvents and other chemicals toxic to the visual system.

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