

# Audition and exhibition to toluene - a contribution for the theme

## Audição e exposição ao tolueno - uma contribuição para o tema

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### SUMMARY

**Introduction:** With the technological advances and the changes in the productive processes, the workers are displayed the different physical and chemical agents in its labor environment. The toluene is solvent an organic gift in glues, inks, oils, amongst others.

**Objective:** To compare solvent the literary findings that evidence that diligent displayed simultaneously the noise and they have greater probability to develop an auditory loss of peripheral origin.

**Method:** Revision of literature regarding the occupational auditory loss in displayed workers the noise and toluene.

**Results:** The isolated exposition to the toluene also can unchain an alteration of the auditory thresholds. These audiometric findings, for ototoxicity the exposition to the toluene, present similar audiograms to the one for exposition to the noise, what it becomes difficult to differentiate a audiometric result of agreed exposition - noise and toluene - and exposition only to the noise.

**Conclusion:** The majority of the studies was projected to generate hypotheses and would have to be considered as preliminary steps of an additional research. Until today the agents in the environment of work and its effect they have been studied in isolated way and the limits of tolerance of these, do not consider the agreed expositions. Considering that the workers are displayed the multiples agent and that the auditory loss is irreversible, the implemented tests must be more complete and all the workers must be part of the program of auditory prevention exactly displayed the low doses of the recommended limit of exposition.

**Keywords:** noise, occupational, toluene, hearing loss, noise-induced, workers.

### RESUMO

**Introdução:** Com os avanços tecnológicos e as mudanças nos processos produtivos, os trabalhadores estão expostos a diferentes agentes físicos e químicos em seu ambiente laboral. O tolueno é um solvente orgânico presente em colas, tintas, óleos, dentre outros.

**Objetivo:** Comparar os achados literários que evidenciam que trabalhadores expostos simultaneamente a ruído e solventes têm maior probabilidade de desenvolverem uma perda auditiva de origem periférica.

**Método:** Revisão de literatura a respeito da perda auditiva ocupacional em trabalhadores expostos a ruído e tolueno.

**Resultados:** A exposição isolada ao tolueno também pode desencadear uma alteração dos limiares auditivos. Estes achados audiométricos, por ototoxicidade a exposição ao tolueno, apresentam audiogramas semelhantes ao por exposição ao ruído, o que torna dificultoso diferenciar um resultado audiométrico de exposição combinada - ruído e tolueno - e exposição apenas ao ruído.

**Conclusão:** A maioria dos estudos foi projetado para gerar hipóteses e deveria ser considerado como passos preliminares de uma pesquisa adicional. Até hoje os agentes no ambiente de trabalho e seus efeitos têm sido estudados de maneira isolada e os limites de tolerância destes, não consideram as exposições combinadas. Considerando que os trabalhadores estão expostos a múltiplos agentes e que a perda auditiva é irreversível, os testes implementados devem ser mais completos e todos os trabalhadores devem fazer parte do programa de prevenção auditiva, mesmo expostos a baixas doses do limite de exposição recomendado.

**Palavras-chave:** ruído ocupacional, tolueno, perda auditiva provocada por ruído, trabalhadores.

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## INTRODUCTION

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With the technological advances and the changes in the productive processes, the workers are displayed daily the different physical and chemical agents in its labor environment, which - in one number significant of situations - finishes for being to revert at risk to the health. This picture is presented still more unsafe when the prevalence of these risks turns it agreed exposition of these products to the noise.

In the last few decades, the occupational auditory losses have been argued in scientific publications, constituting a problem of important health in our society. However, studies appear on other agents, beyond the presence of the noise in environments of work of innumerable productive processes, that agreed, represent a potential risk to the hearing (1).

Amongst main ototoxic chemical composites, can be detached metals, suffocating and the solvents, considering this last group, most present in the half industrials. The toluene is solvent an organic present in glues, inks, oils, amongst others, and its evaluation in the labor environment is through its urinary bioindicator (examination of acid hippuric) (2).

In this article, we will present studies of the effect combined between noise and toluene, in intention to extend the knowledge how much to the effect of the concomitant exposition between the solvent and noise.

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## REVISION OF LITERATURE

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The human being exposition to the toluene occurs from the occupational use, in the domestic environment, through the inhalation with abuse ends and of the ambient exposition. The biggest source of ambient exposition to the toluene is the production and use of the gasoline. Great amounts of toluene are introduced in the environment annually through the use of the gasoline and the production and processes of oil refinement. To calculate the levels of exposition human being proceeding from air, the ground and the water can be difficult (3).

In the last few decades, the occupational auditory losses have been argued ostensive in the half academic for the fact, unquestionable, to consist in a problem of important health in our modern society. However, more recent studies disclose that the presence of chemical agents, in association to the noise make to boosting the loss of hearing in the work environment (1).

The adverse effect of organic solvents in the health had been described in many studies (4, 5, 6). The decreases or moderate concentrations in air, organic solvents can cause temporary symptoms as euphoria, migraine, and vertigo (7, 8) whereas, in raised levels more can lead the cardiovascular anesthesia, problems and illnesses of the respiratory ways (6). The exposition of long stated period can still cause damages for the Central Nervous System as Cognitive Deficits and Emotional, what it would harm good a practical of the worker in its occupational environment, exactly that in simple tasks (9).

The toluene is a aromatically hydro-carbon, liquid and colorless, with characteristic odor, derivative of the tar of the mineral coal and the oil, used as solvent for inks, in the production of explosives, dyestuffs, medicines and detergents and as solvent industrial for rubber and oils and still in the production of other chemistries (10). It is widely used in the graphical industry. It is one of the components of the glue of shoemaker and the gasoline. This last one corresponds the main source of atmospheric emission and exposition of the population in general.

The Toluene is a solvent used of ample form in processes of anthropic transformation, particularly as solvent. In this condition, the related aromatically chemical product can, given to the degree of volatileness in conditions standard of temperature and pressure - 25°C and 1atm - to arrive bigger impacts to the human being, revealed in the form of irritation of the skin and the mucosa. The acute effect of the toluene are similar those derive from the ethanolic poisoning, propitiating a picture of stimulation followed of depression of Central Nervous System (SNC). Already in situation of chronic exposition the risks are of hepato-toxicity, nephrotoxicity and auditory loss (5, 11).

The mechanisms of action of ototoxic substances cause functional damages or cellular damages in the internal ear, mainly in the final structures of the hearing and balance, acting first to the level of the cerebral trunk or in the auditory ways central offices (12).

When is about the auditory loss properly said, the characteristics of the audiometric curve of a attacked patient of exclusive exposition the noise or of another one, with confirmed diagnosis of ototoxicity are sufficiently similar. This because both the pictures are of sensorineural origin, denote cochlear injuries, tend to be irreversible, high frequencies attack initially (acute sounds) and almost always are bilateral (2).

The ototoxic effect of the chemical agents - and amongst these, of solvent the organic ones - has configured in subject of inquiry of great number of researchers.

The NIOSH identified the emergent necessity to establish safe limits for agreed chemical substance exposition and noise (13). European consists of Directive 2003/10/EC that establishes requirements of minimum security in the health of displayed workers the risks, that the employer will have simultaneously to give to particular attention for displayed workers the chemical agents and noise, when leading in account the risk evaluation (14).

The bridge most significant of available literature on the effect of the Toluene in the Auditory System happens essentially of two origins: cases where the patients inhaled the solvent voluntarily (15) and of lead laboratorial experiments with animals. These studies evidence that the exposition to high concentrations of Toluene, for the different ways of administration (verbal, subcutaneous or inhalation) accent the auditory loss. In complementary way to this thesis, in the studies carried through in animals, it was possible to notice great synergism between this solvent and exposition to the noise.

Such conclusion is corroborated by experimental evidences with animals, where the inhalation to high levels of toluene harms the auditory system and causes loss of the audible thresholds.

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## DISCUSSION

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With the growth of the productivity and the advance of the technology, the risks of accidents and illnesses of occupational origin had increased and given origin to some harmful effect to the quality of life, to the individual and collective security of the worker.

In a study with 151 workers of the sector of rotogravure of a graphical industry of São Paulo, displayed simultaneously the noise (85-94dB) and toluene (78-390 ppm), the agreed effect of the simultaneous exposition to both was investigated the agents on the hearing and the balance (16).

In this study, using tests of hearing and balance, the workers had been divided in three groups: displayed the noise and toluene, displayed only the noise and without exposition. In the found results, the percentage of the auditory loss observed in the displayed group the two agents was significantly bigger of what in the others two groups.

Moreover, the measures of the consequence of the acoustic muscle had suggested that the joined auditory losses in this group were significantly different of the ones of the displayed group to the noise, over all with respect to probable localization of the injury. One more time here,

the percentage of imperfections in the balance selection was significantly bigger in the group of workers displayed to both the agents.

Still in the same line of research, another study leads an inquiry with organic solvent and noise, observing its occupational effect. The searched individuals were all workers of rotogravure industry, of the masculine sex, with more than one year of company (17).

As mechanism of collection of data the audiometric examination and immittance testing had been used, beyond questionnaire (age, time of work, chemical time of exposition the noise and products, diabetes, hypertension, infection of ear, ototoxic medicine use, activities of leisure with noise, military service).

The workers had been divided in four groups: 50 displayed workers without any type of exposition, 50 workers with exposition alone the noise (88-97dB), 51 workers the noise (88-98 dB) and toluene (100 ppm) and 39 different displayed workers the mixture of solvent (the component greater of these mixtures was the toluene).

The results had shown to prevalence of bigger auditory loss in the group with simultaneous exposition the noise and toluene (53% in the group with exposition the noise and toluene, 8% in the group without exposition, 26% in the group with exposition only noise and 18% in the group with different exposition the mixture of solvent). In the results of the examinations of immittance testing, was met conscription presence, mainly in the groups of displayed workers to the noise and to the noise and toluene.

In the year of 1993, another study investigated workers displayed to an average concentration of 97ppm of solvent, that had presented absolute latencies and greater interpeaks in the waves in intervals I-III-V in the PEATE in relation to not displayed. With these data, one suggested that the alterations caused for the toluene can be situated in the region of the brainstem and auditory ways central offices. All the individuals of this study had normal audiometry and absence of related symptoms the exposition the solvents (18).

In one another study with solvent and noise inside of the demanded limits, in a producing company of packings with approximately 800 employees, the presented results had not shown boosting of effect. Occurrence of auditory losses in displayed workers only the solvents had over all called the young attention and workers e with little time exposition. In this research one used of the audiometry examinations and immittance testing, and the collaborators had been separate and three groups: exposition only to the

noise, exposition only to solvent and the agreed exposition (19).

In experiments with animals, were used diverse pairs of solvents and the incidence of the interactions of not additive ototoxic. Male rats of the race Long Evans had been used in places where doses of solvent (10% of concentration) were managed per 5 days of 8:30 16:30 hours of Monday a Friday. The effect were compared of 2 the 13 days after the exposition and the auditory function was gotten in the following week of exposition using BERA (reply of potential evoked in the brain). The solvents used had been trichloroethylene (TCE), toluene (TOL), mixing xylene (XYL) and chlorobenzenes (CBZ) and the combination was TOL+TCE, XYL+TCE, XYL+CBZ, CBZ+TOL (20).

For results these authors had gotten evidences of that the combination in way dose-additive of the ototoxic solvents in the effect of the hearing of the rats. In the study with CBZ+TOL the effect had developed throughout the week and not immediately. The threshold of the displayed group was of 10dB bigger of what in the group of control.

According to authors, exactly with the gotten results, cannot conclude that the solvents always will be agreed additively in its effect in the hearing; therefore get synergism when the toxic effect of the agreed expositions is bigger of what the addition of the observed effect.

In a study with rats with long exposition to the toluene for inhalation had presented found suggestive of injuries in the central initial system without evidences of injuries in the peripheral initial function (21).

With the objective to study the effect of the toluene in the structure and function of the Auditory System, it is applied tests of potential evoked (BERA - evaluation of the cochlea) in adult rats of the masculine sex, of changeable average weight between 450-500g, and created in laboratory. The experiment had beginning when the offspring reached the limit of 200 days of life, lasting for understood changeable interval between 3 and 4 months. Completed the sixth month of age the animals had been confined in individual boxes, isolation condition in which had been kept per the 30 days that had preceded the beginning of the experimental process (22).

After to be sedated received electrodes capable to measure their evoked potentials the rats had been submitted the changeable dosages of vapors of toluene with concentrations, respectively of 1000, 1250, 1500, 1750 and 2000 ppm, for a regular period of 6 daily hours, during five days of the week, throughout 4 months.

The gotten results had indicated that only three of the dosages of toluene that the animals had been submitted - of 1500ppm, of 1750ppm and of 2000ppm - had produced confirmed alteration of auditory threshold. The exposition to the toluene resulted in significant auditory deficit in the amplitude of the average frequency (8-24KHz) of the adult rats. The gotten result showed an alteration to cochlear, for the inhalation of the toluene and the main found was the cochlear trauma located in the way of organ of Corti (16-20 KHz) and half it for the apex (4-5 KHz).

Other authors had searched the effect of the simultaneous exposition of the toluene (2000 ppm) and of the noise (92 dB) in rats. These animals had been displayed to the toluene during 6h/day, 5 days of the week, for the period of one month. The results had shown the harmed induction of auditory, external loss hair cells and damaged stereocilia with bigger predominance in the rats displayed simultaneously to the noise and the toluene. The cochlear damage induced for the toluene or noise was caused by two different mechanisms, poisoning and mechanic (23).

With all the existing information and scientific results until then, new research had shown again to the occupational effect of the exposition of workers to solvent and the noise of an rotogravure industry, adding the calculation of the concentration of these mixtures in air and the examination of hippuric acid. 124 workers had participated of the study with solvent exposition to the mixture of acetate (mainly toluene, ethanol and ethyl) and different levels of noise. A questionnaire with all the workers were made (historical of work, psychosocial aspects, chemical medicines, health in general, exposition the noise and products), audiometry examination and immittance testing. Piss of these employees after hours of working was also harvested, for examination of hippuric acid (24).

The results of the audiometry had pointed 49% of the workers with bilateral auditory loss and the immittance testing results had suggested auditory upheaval central or to retrocochlear in the majority of the workers. The results had also shown alteration of the examination of hippuric acid in 95% of the workers. With this, worsening of the auditory loss was suggested, when the worker also is displayed to the toluene (from the data of acid hippuric) and 4 times more possibilities of auditory loss in workers with exposition the toluene and noise. The concentration of toluene in the air did not present significant relation with the auditory loss of the workers and with the results of hippuric acid.

In the evaluation of 64 rats displayed the toluene and ethanol, was divided the animals in 3 groups with exposition and a group of control. The first group was

displayed toluene vapors (1750 ppm, 6 hours per day, 5 days of the week for 4 months). As the group was displayed to ethanol (4g/kg for 4 months), which was injected way displayed gastric intubation and later in surrounding air for 6 hours; e the third group was displayed simultaneously to the toluene and ethanol (ethanol was injected before the exposition to the toluene). Examination of hippuric acid in the animals displayed to the toluene was realized. Piss was collected in 1<sup>o</sup> day and later each 4 days. No drunk or food was given to the animals during the exposition (25).

The results had shown that the auditory loss is more frequent in the exposition the toluene and ethanol of what only the toluene. Ethanol pure modifies the metabolism of the toluene. Auditory loss in the isolated exposition to ethanol was not evidenced.

The cochlea of displayed rats was also evaluated to the toluene, from the examination of Electrocochleography. The study was developed using two groups with each one 8 adult rats. The first group was displayed toluene vapors (1750 ppm) during 6h per day, 5 days of the week, for 4 months and second hand it did not have exposition (26).

After this period of exposition, was realized the examination of Electrocochleography and the results had not only shown alteration of located auditory cells in the portion of lower middle frequencies of the cochlea and in medium frequencies. Thus the lost cells of the Cochlea were concentrated in the region of low medium frequencies and suggested relation of auditory loss with the exposition to the toluene.

In one another study with transitory otoacoustic emissions evoked (EOAET) and the suppression effect, a displayed group was observed the noise and toluene, comparing with a group only displayed with the noise and one another one without exposition. Had been evaluated 140 collaborators with age enter 18-48 years with normal results of audiometric and immittance testing (27).

The prevalence of absence of answers in the EOAET in at least one of the ears was bigger in the displayed group the noise and toluene (64%) and in the displayed group only the noise (62%), that in the group not displayed (27.5%).

The prevalence of absence of the effect of suppression in the displayed group the noise and toluene was bigger (48.9%) in relation to displayed the noise (17.4%) and not displayed (7,5%).

The risk of absence of suppression in the group noise and toluene was significantly bigger when was

compared with the other groups. The results suggest the existence of a neurotoxicity action of the toluene on the a hearing affecting particularly the portion to retrocochlear of the auditory way and causing a type of distinct injury of that one provoked by the noise.

In research on the effect of the surveyed noise and mixture of solvent by means of audiometry of high frequencies, was observed worse thresholds in the comparison of the auditory thresholds in the high frequencies of the displayed group the noise simultaneously and mixes of solvent. This difference was significant for the high frequencies, whereas the results of the thresholds tested in conventional audiometry had not shown significant differences (28).

Was also searched the mixture of solvent alterations in the Evaluation of the Central Auditory Processing in a group of displayed workers. 10 displayed workers to the mixture of solvent and 10 works not displayed had participated of the study, with results of audiometry and immittance testing inside of the normality standards (29).

The findings of the central auditory processing had been lower in the displayed group the mixture of solvent, suggesting that, exactly without presenting alteration in the auditory examination, diligent displayed the mixture of solvent they present difficulties with the daily questions, what was proven with the auditory alterations central offices presented in the processing test.

In the evaluation of the risk of auditory loss in workers of a displayed adhesive industry the noise and toluene, divided the workers in 3 groups: in the first group, 58 workers had been displayed the noise (78.6-87.1dB) and toluene (33,0 ppm, 107,6 ppm and 164,6 ppm); in the second group, 58 workers only displayed the noise (67,9 - 72,6dB); e in the third group, 60 workers of the administrative sector, that did not have any type of exposition, serving of group of control (30).

All had answered to a questionnaire with information of health and style of life and had carried through audiometric examination. The tests had been carried through 14 hours after the ending of the day. The percentage of the auditory loss was calculated from the result of the worse ear. The displayed group the noise and toluene was subdivided in other groups, leading in consideration the level of the noise. Approximately 28% of the displayed workers the noise and toluene worked have more and 20 years. The predominance of the noise concentrations had been: sector noise and toluene: 83,9dB; sector noise 85,0 dB and 70,0 in the administrative sector. But 15% of the displayed workers the noise used EPI. The prevalence of the auditory loss was very bigger in the

group of noise and toluene (86.2%) in relation to the group displayed only to noise (44.8%) and 5% in the administrative group.

In research with expositions the inks and noise, studied painting sectors of automobiles of two companies and verified effect aggravation of the exposition the inks on the auditory thresholds of displayed individuals the noise between 81 and 85dB. The auditory losses verified in the displayed group the noise and inks was similar observed in the group only displayed the noise between 92-107dB (31).

In the evaluation of the effect of the solvent exposition the noise and on the peripheral auditory ways and central in workers of a graphical industry of Guarulhos in the period of September/2004 to August/2005, observed solvent association of the exposition of organic (gasoline, 3 n-hexane and thinner) and the alteration in the central auditory way was verified by means of the result of the test of the evoked potential auditory of long P300 latency (PEAL-P300) (32).

The research was realized with 136 workers and the prevalence of auditory losses found in the displayed group the noise and solvents (23.3%) was considerably bigger than in the others 2 groups, not displayed (8%), only displayed the noise (12.5%), only displayed the solvents (20%).

The results of the study suggest that the exposition to the noise had greater repercussion on the auditory threshold and the exposition to the solvents showed strong association with alterations in the results of the PEAL-P300.

Studies as the described before, in its majority carried through with animals created in laboratories, show to the effect of solvent the agreed exposition or not to the noise and (in this in case that, the toluene) and the different methods of evaluation of the auditory system.

All the realized analyses of association had indicated that the expositions, agreed or not, associate cases of auditory losses. The results had suggested that the exposition the high concentrations of mixtures of solvent and to the toluene in a noisy environment, can increase the risk significantly to acquire a occupational auditory loss. The results of the immittance testing had also suggested alteration of the central auditory system.

The tests of audiometry and immittance testing used in the studies are not enough to evaluate the effect of solvent to the hearing. The other used methods of evaluation, in show to the importance of a complete

battery of audiological examinations for determination of the place and type to them of injury.

These other tests had shown that the ototoxic solvents damage the hair cells of the cochlea, suggesting that the toluene can damage cellular membranes selectively. The external hair cells, that facilitate the codification of the auditory information for the motor process of the cochlea, had been the targets most frequent of the ototoxic ones.

It cannot be conclude, however, if the solvents always will be agreed additively in its effect in the hearing. The infinity of products and the different concentrations hinder a trustworthy evaluation of its effect. The induced traumas for solvent would not be caused by the contamination of the fluid, but by poisoning of the fabric involving the ridge external, instead of the auditory nerve (20, 33).

The results had also suggested the existence of a neurotoxicity action of the toluene on the hearing affecting particularly the portion to retrocochlear of the auditory way and causing a type of distinct injury of that one provoked by the noise. The register of the EOAET and the analysis of the suppression effect can serve with instrument important in the precocious detention of the auditory alterations of origin to cochlear and to retrocochlear and for the elaboration of preventive actions in audiological in work environments (27).

In Table 1, it meets description of main described articles above, in summary, on the mixture of solvent and noise.

## FINAL COMMENTS

Until today the agents in the environment of work and effect they have been studied in isolated way and the limits of tolerance of these, do not consider the agreed expositions. Considering that the workers are displayed the multiples agent and that the auditory loss is irreversible, the implemented tests must be more complete and all the workers must be part of the program of auditory prevention exactly displayed the low doses of the recommended limit of exposition. Studies on the ototoxic effect of the toluene in the occupational exposition are not conclusive yet.

It is important to remember that, as for the noise, the simple presence of the studied ototoxic agent (in the case the toluene), is not synonymous of exposition. So that some type of effect in the auditory agency occurs, the absorbed dose, that depends, among others, of the levels of concentrations in the environment and of the time of exposition, must be enough to cause the effect

**Table I . Solvent article description on mixture of (including the toluene) and noise:**

Year	Article	Authors	Exposition	Objective	Method	Results	Conclusion
1990	An epidemiological study of the effects of exposure to noise and organic solvents on workers' hearing and balance	Morata, TC	Noise and toluene	To investigate the effect of the simultaneous exposure to noise and toluene on the hearing and balance of workers	Interviews and tests of applied hearing and balance in 3 groups of workers in one Graphical Industry of São Paulo. Total: 151 workers. The hearing and the balance of a printer group of the sector of displayed toner was the noise (85-94db) and toluene (78-300 ppm) had been simultaneously compared with a group of printer displayed only the noise (87-88db) and with one third group not displayed the noise or toluene.	The percentage of auditory loss observed in the displayed group the 2 agents were significantly bigger of what in the 2 other groups. Moreover, the measures of the consequence of the acoustic muscle lead suggested that the joined auditory losses in this group had been significantly different of the ones of the displayed group the noise, with respect to probable localization of the injury. The percentage of imperfections in the balance selection was significantly bigger in the group of workers displayed to both the agents	The results suggest that the exposure to the high concentrations of toluene in a noisy environment can increase in significant way the risk to acquire one deaf auditory occupational and that the high noise cannot more considered being as only threat the hearing of the workers.
1993	Effects of occupational exposure to organic solvents and noise on hearing	Morata, TC et al	Solvent organic and noise	To investigate solvent the occupational effect of the exposure organic and noise of workers of a tonerware industry, of the masculine sex and with more than 1 year of company	Audiometric examination, immitance testing and questionnaire (age, time of work, time of exposition the chemical noise and prods, diabetes, hypertension, infection of ear, ototoxic medicine use, activities of leisure with noise, military service) Workers divided in four groups: 50 workers with lesser exposure 85dB, 50 displayed workers with exposure alone the noise (88-97dB), 51 workers the noise (88-98 dB) and toluene (100 ppm) and 39 different displayed workers the mixture of solvent (the component greater of these mixtures was the toluene).	Audimetry: Prevalence of bigger auditory loss in the group with simultaneous exposure the noise and toluene 53% group exposure noise and toluene, 8% group without exposure, 26% group exposure noise, 18% group solvent exposure mix. Immitance testing: conduction presence, mainly in the groups of displayed workers the noise and the noise and toluene.	- Existing synergism between noise and solvent - the audiometric test is not only enough for the evaluation of displayed workers the noise and solvent - resulted of the acoustic consequences they suggest alteration of the Central Auditory System - the used tests in this study (audiometry and immitance testing) are not enough for the study of the effect of solvent to the hearing. It is necessary a complete battery of audiological examinations for determination of the place and type of injury.
1993	Neurotoxicity induced by exposure to toluene	Alhara, C., Gorgianni, C., Manna, F. Brecciarini, R.	Solvents	To evaluate workers displayed to toluene and not displayed, making use of the PEATE.	Examination PEATE in displayed the average concentration of 97 ppm of toluene and not displayed workers	Workers displayed to an average concentration of 97 ppm of solvent, lead presented bigger absolute latencies and interpeak in the waves in intervals III-V in the PEATE in relation to not displayed, suggesting that alterations caused for the toluene can be situated in the region of the brainstem and auditory ways central offices.	All the individuals of this study had audio normal and absence of related symptoms the exposure the solvents, what it indicates the importance of other tests beyond the audiometry, in solvent the displayed and the noise group.
1994	Auditory effect provoked by the interaction between noise and solvent. A preventive boarding in audiology directed the health of the worker	Souza, M.I.	Solvents and noises	To evaluate solvent displayed workers, the noise and solvent and noise (agreed exposition).	Group of workers displayed only the noise, only solvent and the two. Carried through audio and immitance. Study in a company of packings with approximately 800 employees. Noise and solvent inside of the demanded limits.	Boosting of effect was not observed, however occurrence of auditory losses in displayed workers only met the solvents (these the youngest workers were e with little time of exposition).	The minority of products and concentrations hinders a trustworthy evaluation of its harmful effect.
1995	Combined effects of paired solvents on the rat's auditory system	Robert, CS, Schwartz, RW, Swendsgaard, D.L, Pryor, GT e Bines, WK.	Several pairs of solvents	To determine the incidence of interactions of not ototoxic additives between some pairs of solvent	Solvent used: mixing trichloroethylene (TCE), toluene (TOL), xylene (Xyl) and chloroformers (CBZ). The combination was TOL+TCE, Xyl+TCE, Xyl+CBZ, CBZ+TOL. One used male rats of the open Long Evans where the odor of the solvents (10% of concentration) was managed per 5 days of 8:30-16:30 hrs of 21/61. The effect were compared of 2 the 13 days after the exposition and the auditory function was gotten in the following week of exposition using DEBA (reply of potential evoked in the brain).	The results had shown that the solvent used ototoxic had combined in way dose-additive in the effect of the hearing of the rats. In the study with CBZ+TOL the effect had developed not immediately throughout the week and. The threshold of the displayed group was of 10dB bigger of what in the group of control.	The ototoxic solvents damage the hair cells of the cochlea. One has suggested that the toluene can selectively damage cellular membranes, for interrupting the way ATPase that differently are distributed in the external and internal hair cells and throughout the fundamental membrane. If it cannot conclude however, that the solvents always will be agreed additively in its effect in the hearing, they are gotten as additively the toxic effect of agreed exposures predicted by an arithmetical addition of the individually observed effect and gets synergism when the toxic effect of the agreed exposures is bigger of what the addition of the observed effect.
1995	Function of the auditory system, the visual systems and peripheral nerve after long-term combined exposure to toluene and ethanol in rats	Nylen, P., Hagman, M., Johnson, AC	Toluene and Ethanol	To evaluate the hearing of displayed rats toluene and ethanol	Study with rats with long exposure to the toluene for inhalation	Findings had been suggestive of injuries in the central initial system without evidences of injuries in the peripheral initial function.	

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1996	Toluene-induced Hearing Loss: a Mid Frequency Location of the Cochlear Lesions	Campo, T. et al	Toluene	To study the effect of the toluene in the structure and function of the Auditory System, from tests of potential evoked (av cochlea) in adult rats.	Rats of the masculine sex had been used, created in a laboratory of France. These weighed between 450-500g and the experiment was initiated when had 7 months of age and enters 10-11 age months the experiment arrived at the end. The rats had been in individual boxes of polycarbonate, one month before the experiment. The animals had been anesthetized, verified the auditory conduit, in intention to exclude any alteration of external and average ear and introduced electrodes for evaluation of 1000, 1500, 1750 and 2000, 60 per day, 5 days of the week, for 4 months.	But these values of toluene concentration (1500, 1750 and 2000) had produced mean alteration in the results of the toluene threshold auditory produced significant an auditory deficit in the amplitude of the average frequency (8-24kHz) of the adult rats. The histological data demonstrate that the toluene has toxic effect in the cochlea, as the loss of hair cells and intra ganglionic space their absence.	- The gotten result showed an alteration to cochlear, for the inhibition of the toluene for rats of the masculine sex and in the band of 7 the 11 months of age. - The main finding was the trauma to cochlear located in the way of agency of Corti (16-20 kHz) and half of for the apex (4-5 kHz). - The BEPPA was the used examination for this experiment.
1997	Correspondence between middle frequency auditory loss in vivo and outer hair cell shortening in vitro	Lin, Y, Rao, D. e Fechter, L.D.	Toluene	To demonstrate that the exposition of the toluene in vitro produces morphologic changes in the external hair cells (reduction) and a effect on the cells of the half of the apex of the cochlea.	They show in a study with 15 pigs of the Guinea, that the exposition to the toluene, with a concentration a little above of the allowed level, produces morphologic changes in the external hair cells (reduction) and a effect on the cells of the half of the apex of the cochlea.	The reduction of the cells happened in first the 15 minutes of exposition and had its apex to the 55 minutes. The basal cells (high frequency) in the portion of the cochlea had lost after about 15% of its initial length 60 minutes of exposition. According to these same authors, the external hair cells, which facilitate the codification of the auditory information for the motor process of the cochlea, are while more frequent of ototoxic.	The external hair cells are while more frequent of ototoxic. They facilitate the codification of the auditory information for active the motor process of the cochlea.
1997	Combined effects as simultaneous exposure to noise and toluene on hearing function.	Laraya, R. e Campo, P.	Toluene and Noise	Effect of the toluene in set with the effect of the noise, making simultaneous exposition of both.	Rats. Exposition to the toluene (2000 ppm) per 6hr/day, 5 days of the week, during 1 month. Noise 92 db.	The exposition to the toluene in the rats induced auditory loss and the histological data had indicated that the external hair cells are more sensible. The exposition to the noise induced auditory loss and the histological data show the damaged stereocilia. The damage to cochlear induced for the toluene or noise is caused by two different mechanisms, poisoning and mechanic. The rats displayed to the noise and the toluene had simultaneously suffered more severe auditory loss.	There is a coexistence of both mechanisms to boosting the effect of the cochlea.
1997	Toluene-induced hearing loss among micrograve printing workers	Morara, T. et al	Solvents and Noise	To study the occupational effect of the exposition of workers solvent and the noise of an industry and microgravees.	The mixture of (mainly toluene, ethanol and ethyl) had participated of the study 124 workers with solvent exposition acetate) and different levels of noise also Calculated the concentration of these mixtures in air. A questionnaire with all was carried through the workers (historical of psychosocial work, aspects, chemical medicines, health in general, exposition the noise and products), examination of audiology and immittance testing. Piss of these employees after hours of working was also harvested, for examination of hippuric acid.	- 49% of the workers had presented bilateral auditory loss - the concentration of toluene in air did not present significant relation with the auditory loss of the workers and with the results of hippuric acid - resulted of immittance testing - they suggest auditory upheaval central or to retrocochlear in the majority of the workers - resulted modified of hippuric acid in 95% of the workers.	- The solvent noise is suggested more complete audiological examinations for the evaluation of the hearing of displayed workers and (audio tonal, vocal, immittance testing and initial tests) - worsening of the auditory loss is suggested, when diligent is also displayed to the toluene, from the data of hippuric acid of these. - The worker with exposition the toluene and noise has 4 times more possibilities of auditory loss - The recommendation of the exposition limits the chemical products are not adjusted when more exposures exist.
1998	Combined Effects of a Simultaneous Exposure to Toluene and Ethanol on Auditory Function in Rats	Campo, P. et al	Toluene and Ethanol	Auditory evaluation of displayed rats the toluene and ethanol.	64 rats divided in 3 groups with exposition and a group of control had participated of the study. The first group was displayed toluene vapors (1750 ppm, 6 hours per day, 5 days of the week for 4 months). As the group was displayed to ethanol (4g/kg for 4 months), which was injected very gastric intubation and later displayed in surrounding air for 6 hours and the third group it was displayed simultaneously to the toluene and ethanol (ethanol was injected before the exposition to the toluene). Examination of hippuric acid in the animals displayed to the toluene was realized. Piss was collected in 1 <sup>st</sup> day and later each 4 days. No drunk food or was given to the animals during the exposition.	Pure ethanol modifies the metabolism of the toluene. The auditory loss is more frequent in the exposition the toluene and ethanol of what alone the toluene. Auditory loss in the isolated exposition to ethanol was not evidenced.	Pure ethanol modifies the metabolism of the toluene. The auditory loss is more frequent in the exposition the toluene and ethanol of what alone the toluene. Auditory loss in the isolated exposition to ethanol was not evidenced.



1999	Toluene Ointoxicity in Rats: Assessment of the Frequency of Hearing Defect by Electrocochleography	Lataye, R., Campo, P., Lomet, G.	Toluene	To evaluate the Cochlea of displayed rats the toluene, from the examination of Electrocochleography.	The study was developed in a Laboratory on France and used 2 groups of 8 adult rats. The first group was displayed toluene vapors and second hand it did not have exposition. The animals approximately had between 350-420g and 4 months of age. The animals of the first group had been displayed vapors of toluene of 1750 ppm, during 6h per day, 5 days of the week, for 4 months. Only after this period of exposition, the examination of Electrocochleography was realized.	The examination not only showed alteration of located auditory cells in the portion of lower middle frequencies of the cochlea and in medium frequencies.	The examination of Electrocochleography not only showed an alteration in the medium frequency of 16KHz, but also in the medium frequency decrease of 4kHz. Thus the last cells of the Cochlea were concentrated in the region of low medium frequencies. Relation of auditory loss with the exposition to the toluene is suggested.
1999	Comparison of toluene induced and styrene induced hearing losses	Lataye, R., Campo, P., Lomet, G.	Styrene and Toluene	To compare the effect of the toluene and the styrene in the auditory system of rats.	96 rats with 450-500g and 4 months of age had participated of this study. One used doses of 1000-2000 ppm toluene and 500-1500 ppm of styrene (exposition of the vapor: 6 hours per day, 5 days of the week, for 4 consecutive months). The auditory system was tested Prie examinations of potentials evoked in freq of 2 - 32 kHz	- Similar results of curve, with concentration of 1750ppm of toluene and 850 ppm of styrene, in freq of 12,10,20 and 24 Hz - the effect of the toxicity of the toluene start with concentrations of 1360 ppm and 570 ppm of styrene - preserver alterations in the agency of corti and cells - the two solvents have similar toxic effect	- Exposition the toluene and styrene cause permanent auditory loss in rats. - The styrene has a bigger toxic effect of what the toluene - Toluene and styrene dangerous industrial for the hearing of adult rats are solvent. - Hair Cochlea and some cells are the affected structures more.- Styrene concentrations are 2 times more harmful than of toluene
1999	Toluene and styrene intoxication route in the rat cochlea	Blaichere, V., Campo, P., Lomet, G. e Roue, M.	Toluene e Styrene	Inquiry of the route of the poisoning for which the solvent reaches the cochlea. (contamination of fluid x poisoning of the fabric)	Use of the toluene (1750 ppm) and styrene (750 ppm) in adult rats long Evens for 10 hours (being consecutive 6 and 4 in the following day). The FCE (fluid spinal brain), blood, brains tissue, auditory nerves, WAS (fluid of the internal ear) and cochlea had been analyzed in such a way for the toluene how much for the styrene using chromatography for gas, giving more approach to the cerebellum and regions of bridge.	The found concentration of solvent in the brain was bigger of what the joined one in the blood. The toluene concentration was of 47,6 mg/g in brain and 26.1 mg/g in 30 blood and 45 and mg/g, 1 hour after of the 4 hours of the exposition of 2000ppm of toluene. The concentration of styrene in the brain was of 68 mg/g and in the blood of 37,5mg/g. These differences of rates found in the blood and the brain: the toluene and the styrene are lipophylic and the fabric cerebral is constituted mainly by rich regions in lipids, compared with the blood. The styrene is more present in the bridge and the cerebellum that are rich in lipids. The toluene and the styrene chemically are not attracted by watery environments. The route of poisoning shown in the study tells that the contamination of the Agency of Corti did not have to it WAS, therefore the solvents hardly is found in this. The authors suggest two probable routes of involved poisoning in the induced auditory loss for solvent: 1º the solvents would spread out of the eighth nerve for the hair cells, because the concentration of solvent is bigger in the nerves that in the blood. However it is difficult to explain the pathological standard of the damage of the Agency of Corti for the solvents (the external hair cells of the third column more are damaged of what the second column and that more it is damaged than the first one). 2º the solvents would be carried by the blood, if they would spread out on the ridge external of the membranes and would reach the cells of Hansen. The last cells are in connection with the cells of Deiter that are located on the external hair cells, and thus the solvents reach the agency of Corti.	The induced traumas for solvent would not be caused by the contamination of the fluid, but by poisoning of the fabric involving the ridge external, instead of the auditory nerve.

2000	Low-level toluene disrupts auditory function in guinea pigs	Mr. Williams, M.L, Chen, GD e Fichter, LD	Toluene	Study of the metabolism of the external hair cells of rats after the exposition low the concentration of toluene	Low toluene concentration 250ppm for 8 hours to the day, 5 days of the week for 1 month	Enzymatic activity reduced in the region of medium frequencies of the cochlea was found after exposition the low concentrations of toluene.	The alteration of the metabolism of the external hair cells can take the auditory loss and permanent loss of these cells.
2000	Displayed workers simultaneously the noise and toluene: study of the acoustical emissions evoked and effect of suppression	Benarati, A.PA.	Noise and toluene	Study of the transitory acoustical emissions evoked (E0AE) and the effect of suppression in a displayed group the noise and toluene, comparing with the group only displayed with the noise and without exposition	140 individuals with age of 18-48 years with audio and immitance normal had been evaluated.	The prevalence of absence of answers in the E0AET in at least one of the ears was bigger in the displayed group the noise and toluene (6.9%) and in the displayed group the noise (62%) that in the group not displayed (27.5%). The prevalence of absence of the effect of suppression in the displayed group the noise and toluene was bigger (48.9%) in relation to displayed the noise (17.4%) and not displayed (7.5%). The risk of absence of suppression in the group noise and toluene significantly bigger when was compared with the other groups	The results suggest the existence of a neurotoxic action of the toluene on the hearing affecting particularly the portion to retrocochlear of the auditory way and causing a type of distinct injury of that one provoked by the noise. The register of the E0AET and the analysis of the suppression effect can serve with instrument important in the precocious detection of the auditory alterations of origin to cochlear and to retrocochlear and for the elaboration of injunictions in audibility in work environments.
2000	Evaluation of combined effect of organic solvents and noise by the upper limit of hearings	Morioka, J, Miyai, N, Yamamoto, H, Miyashita, K	Noise and mixture of solvent	Study of displayed workers the noise and mixes of solvent by means of audiometry of high frequencies		Comparison of the auditory thresholds in high freq. of the displayed group, simultaneously the noise and mixes of solvents, observed worse thresholds. This difference was statistical significant for the high frequencies, whereas the results of the thresholds tested in conventional audiometry had no shown differences.	
2002	Environment of work a risk place	Sierfen et al	Noise and toluene	To study the auditory damage in displayed workers the noise and toluene in a plant of shoes	During the hours of working of 8 daily hours/ five days of the week, one analyzed the levels of noise and concentrations of solvent which the workers were displayed and effect on the auditory system.	The results had shown that, exactly displayed the levels of noise allowed by Norma Regulation of the country (85 dBA, 8h - NR-15, MT/BR) and lesser concentrations of toluene of what established for this norm (78 ppm), group displayed to the accentuated auditory noise and the solvent was what presented loss more.	With these data, the authors suggest that the exposition to these agents, exactly inside of the allowed limits, can increase the occurrence of auditory losses, being worried about the fact of 8hs of exposition daily and many times without the adequate protection.
2003	Occupational toluene exposure and auditory function: results from a follow-up study	Scheper, M., Demmes, P., Michalski, Z, Blaszkewicz, M, Szewc, A.	Toluene e noise			Evaluating 333 displayed workers the noise and decreases toluene concentrations, the biological pointer (hippuric acid in piss) was not significant.	Exposures the toluene below of 50 ppm do not have to be enough to cause some auditory damage and suggest new studies with noise and toluene in low concentrations.
2004	Effect of chemical products and noise in gesseses of the auditory loss	Anitza Pres de Melho de Azevedo	Noise and solvents	Revison of literature		In field, studies the challenge to analyze that type of interaction occurs between the 2 agents, for the difficulty in locating populations with exposures is enormous equivalents for comparison. Expositions, solvent and noise has more prevalence of auditory loss and exposition alone to some chemical products exactly develops auditory loss in low concentrations.	Neurotoxic products can take or so more serious problems of the auditory loss. It has you evidence of that the auditory loss can be a precocious manifestation of poisoning. Another alarming data are the possibility of this loss to progress, although finish of the exposition the chemical agent. It is remembers, that a neuro-toxic composition can not only injure the peripheral component of the hearing, but also its central component.
2006	Assessment of central auditory processing in a group of workers exposed to solvents	Fuente, A et al	Solvents	Evaluation of the Central Auditory Processing of a group of displayed workers the mixture of solvents.	10 workers not displayed to the solvent mixture and 10 workers displayed to the solvent mixture had participated of the study. The study it was carried through in a laboratory in Santiago, Chile and had been excluded the workers with auditory alterations. To participate of the study, the results of audiometry and immitance testing had to be inside of normality.	All the workers presented examination of normal audiometry and immitance testing; however the findings of the auditory processing had been lower in the displayed group the mixture of solvent.	Exactly without presenting alteration in the auditory examination, diligent displayed the mixture of solvent they present difficulties with the daily questions, what it was proven with the auditory alterations central offices presented in the processing test.

2006	Hearing loss in workers exposed to toluene and noise	Cheng, S. J. et al	Noise and Toluene	To evaluate the risk of auditory loss for displayed workers the noise and toluene.	The workers of an adhesive industry had been divided in 3 groups: in the first group, 58 displayed workers the noise (76.6-87.1) and toluene (33.0 ppm, 107.6 ppm and 164.6 ppm); in the second group, 58 displayed workers only the noise (67.9 - 72.6), and in the third group, 60 workers of the administrative sector. All had answered to a questionnaire with information of health and style of life and had earned through audiometric examination. The tests had been carried through 14 hours after the ending of the day. The percentage of the auditory loss was calculated from the result of the ear worse. The displayed group the noise and toluene was subdivided in other groups, leading in consideration the level of the noise.	Approximately 28% of the displayed workers the noise and toluene worked have more and 20 years. The predominance of the noise concentrations had been: sector noise and toluene: 83, 94B; sector noise 85, 0 dB and 70,0 in the administrative sector. But 15% of the displayed workers the noise used EPI. The prevalence of the auditory loss was very bigger in the group of noise and toluene (66.2%) in relation to the group displayed only to noise (44.0%) and 5% in the administrative group.	Studies on the ototoxic effect of the toluene in the occupational exposure not yet are conclusive. The ototoxic interaction was suggested in 1964 for Flanagan and Axelsson. However the effect depend on the dose and the period of exposure. It is the first study to evaluate the interaction noise and toluene in the hearing human being. This study showed to q the effect caused for the exposure noise and toluene is different in each frequency. However q is only known the exposure to the toluene and to disulfide of carbon it has great effect in the band of frequencies. This study the limit of 100ppm of toluene suggests q more does not protect the auditory health of the worker when displayed to the noise also. Findings of this study and other studies with other solvents, are important to think themselves about new forms of implementation of values of limits for solvent.
2006	Toxic solvents in car paints increase the risk of hearing loss associated with occupational exposure to moderate noise intensity	El-Shazly, A.	Paints and Noise		It was studied two painting sectors of automobiles of two companies and verified effect aggravation of the exposure the noise on the auditory thresholds of displayed individuals the noise between 81 and 86dB. The auditory losses verified in the displayed group the noise and inks the noise between 92- 107dB was similar observed in the group only displayed. The author did not specify if former exposures had been considered.		
2007	Thesis of Doctoral USP - solvent (Occupational Exposition the noise and peripheral auditory alterations and central offices.	Drª Alice Penna Bernardi	Noise e solvents	To evaluate the effect of the solvent exposition the noise and on the peripheral auditory ways and central in workers of a graphical industry.	Association of the exposition of 3 organic solvents (gasoline, n-hexane and thinner) and alteration in the central auditory way by means of the results of the test of the evoked potential auditory of long P300 latency (PEAL-P300). Study with one workers graphical industry of Guanabara in the period of September/2004 to August/2005. At the beginning of the research the company counted on 349 contracted workers. The research was carried through with 136 workers	Workers with maximum age of 50 years for the process of Presbycusis not to intervene with the results. The prevalence of auditory losses found in solvent the displayed group the noise and (23.3%) was considerably bigger than in the others 2 groups, not displayed (8%) and only displayed the noise (2.5%) diligent only displayed the solvents (20%). The results of the study suggest differences in the type of alterations caused for the exposure noise and solvents exposition to the noise had greater repercussion on the auditory threshold and the exposition to the solvents showed to fort association with alterations in the results of the PEAL-P300. Equal results on the FHEME study (2006)	Workers had presented greater probability of solvent peripheral auditory alterations when displayed the noise and. The isolated exposition the solvents in general increased the probability of auditory alterations central offices. The alterations observed in test PEAL-P300 suggest a neurotoxic action of solvent on the hearing intervening with auditory functions in the critical level.
2008	Ototoxicity of Toluene and Styrene: State of Current Knowledge	Huel, P. and Lison, D.	Toluene e estirano	Revision of literature of the ototoxic effect of the toluene and the styrene in the auditory system.	To see table of comparison of the different studies on styrene and toluene.	Considering that the workers are displayed the multiples agent and that the auditory loss is irreversible, the implemented tests must be more complete and all the workers must be part of the program of auditory prevention exactly displayed the low doses.	

Being thus, is important that the managers and/or professionals who work with the question of the Health of the Worker, is alerted of the effect combined concerning the exposition the noise and chemical substances, so that it can search tools for quarrels of effective norms and the programs of auditory conservation, contributing for more good a management in the health of the worker. The perspective of study of the combined effect, not only of the toluene, but of the majority of the chemical agents, must deserve greater attention so that if it can plan measured adequate of protection, rethink the existing Programs of Auditory Conservation.

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