Chronic Exposure to Neurotoxic Factors and Sense

Assoc Prof **Sibel Kiran** MD PhD
Zonguldak Karaelmas University, School of Medicine,
Department of Public Health;
Health Science Institute;
Center of Workers' Health and Work Safety
Zonguldak-TURKEY

sibelkiran@gmail.com

Outline

- Chronic exposure ?
- Neurotoxic substances ?
- What do we have ? How do we gather data for information? And what is its use?
- Exposure and Effect relationship-- Chronic exposure
- Senses?
- **(Chronic) exposure evaluation for sensory system**
- Any neglect in occupational health practice-evaluation-situation?: importance-possibilities-resources-records-reports?
- What do we need?

Chronic exposure definition?

a. Long term exposure, usually lasting one year to a lifetime. [CARB, 2000: Glossary of Air Pollution Terms];

b. Multiple exposures occurring over an extended period of time, or a significant fraction of the animal's or the individual's lifetime. [IRIS, 1999: Glossary of IRIS Terms];

c. A long term exposure to a chemical for a period of one year or more in animals and more than **seven** years in humans. [OFA, 2000: Oxyfuels Glossary];

d. A persistent, recurring, or long term exposure, as distinguished from acute. Chronic exposure may result in health effects (such as cancer) that are delayed in onset, occurring long after exposure has ceased. [REAP, 1995: Residential Exposure Assessment Project];

e. Multiple exposures occurring over an extended period of time, or a significant fraction of the animal's or the individual's life_time. [USDOE, 2000: RAIS Glossary];

f. Long_term exposure usually **lasting 6 months** to a lifetime. [USEPA, 1995: Benchmark Dose];

g. Multiple exposures occurring over an extended period of time or over a significant fraction of an animal's or human's lifetime (Usually seven years to a lifetime.) [USEPA, 1997a: EPA Terms of Environment];

h. Exposure to the poison occurs over a period of weeks, months, or years; onset of signs may be sudden and dramatic, or can be insidious like a slow loss in body condition or reduced productivity. [WSU, 1999: Definitions and Abbreviations of Veterinary Terms]

ATSDR

Acute = 1 to 14 days,
Intermediate = 15 to 364 days, and
Chronic = 1 year or longer

Neurotoxic Substances

- 1,1,1-Trichloroethane
- 1,1,2-Trichloroethane
- 1,1-Dichloroethene
- 1,2-Dichloropropane
- 1,3-Butadiene
- 2,4- & 2,6-Dinitrotoluene
- 2-Hexanone
- Acetone
- Acrylamide
- Acrylonitrile
- Aldrin/Dieldrin
- Aluminum
- Americium
- Arsenic
- Benzene
- Bis(chloromethyl) Ether
- Bromoform & Dibromochloromethane
- Bromomethane
- Cadmium
- Carbon Disulfide
- Carbon Monoxide
- Carbon Tetrachloride
- Chlordane
- Chlordecone
- Chlorfenvinphos
- Chlorine Dioxide & Chlorite
- Chlorobenzene
- Chloroform
- Chloromethane
- Chlorpyrifos
- Cresols

- Cresols
- Cyanide
- DDT, DDE, DDD
- Diazinon
- DichlorvosDinitrocresols
- Disulfoton
- Endosulfan
- Endrin/Endrin aldehyde
- Ethion
- Ethylbenzene
- Ethylene Oxide
- Fuel Oils / Kerosene
- Gasoline, Automotive
- Heptachlor/Heptachlor Epoxide
- Hexachlorocyclohexane (HCH)
- Hexachloroethane
- HMX (Octogen)
- Hydraulic Fluids
- Hydrogen Sulfide
- Ionizing Radiation
- Jet Fuels JP-4 and JP-7
- Jet Fuels JP-5 and JP-8
- Lead
- Malathion
- Manganese
- Mercury
- Metallic Mercury
- Methoxychlor
- Methyl Mercaptan
- Methyl Parathion
- Methyl tert-Butyl Ether (MTBE)
- Methylene Chloride
- Naphthalene, 1-Methylnapthalene, 2-Methylnapthalen

Otto Fuel II and its Components
Polychlorinated Biphenyls (PCBs)
Pyrethrins and Pyrethroids
Pyridine
RDX (Cyclonite)
Stoddard Solvent
Styrene
Tetrachloroethylene (PERC)
Tetryl
Thallium
Tin and Compounds
Toluene
Trichloroethylene (TCE)
Used Mineral-based Crankcase Oil
Xylenes

ILO
WHO
IPCS
inchem.org
WHMIS
NIOSH, ATSDR
.....
....

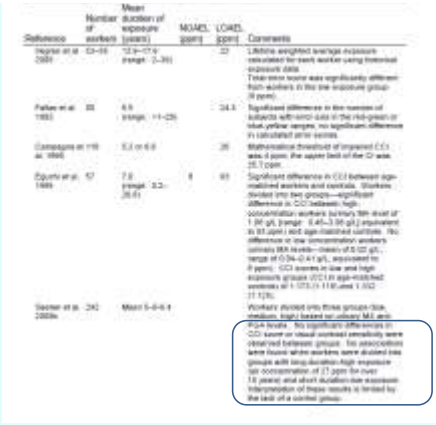
CAS number- MSDS

Styrene
http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=74

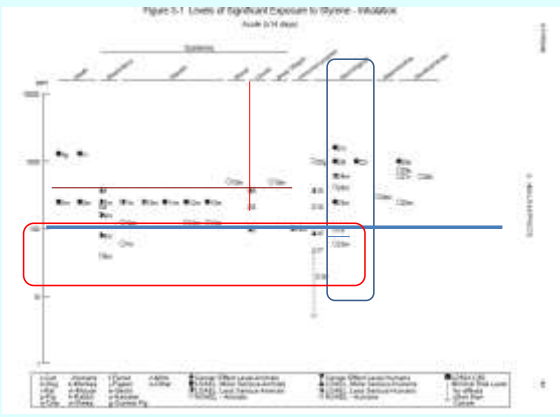
Uses	
• Manufacturing	Large amounts of styrene are produced in the United States. Small amounts are produced naturally by plants, bacteria, and fungi. Styrene is also present in combustion products such as cigarette smoke and automobile exhaust.
• Consumer products	Styrene is widely used to make plastics and rubber. Consumer products containing styrene include: • packaging materials • insulation for electrical uses (i.e., wiring and appliances) • insulation for homes and other buildings • fiberglass, plastic pipes, automobile parts • drinking cups and other "food-use" items • carpet backing These products mainly contain styrene linked together in long chains (polystyrene). However, most of these products also contain a small amount of unlinked styrene.

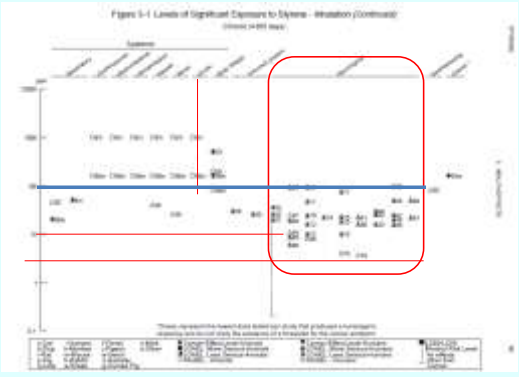
Table 2-1. Results of Selected Human Neurotoxicity Studies

Result	Reference	NOAEL ppm	LOAEL ppm
Decreased color discrimination	Chia et al. 1994		5
	Kishi et al. 2001	4	10
	Gong et al. 2002		10
	Gobba et al. 1991		16
	Triebig et al. 2001		20
	Ingren et al. 2005		22
	Fallas et al. 1992		24.3
	Campagna et al. 1995		25
	Eguchi et al. 1995	8	83
Neurological symptoms	Flodin et al. 1989	5	
	Edling et al. 1993	8.6	
	Checkoway et al. 1992	10.8	18.9
	Chevry et al. 1980		62
Vestibular effects	Möller et al. 1990		18
	Trapido et al. 2006		24.8
	Calabrese et al. 1996		36
Hearing	Morata et al. 2002		3.68
	Sliwińska-Kowalska et al. 2003		15.6
	Morioka et al. 1999		16
	Möller et al. 1995	18	
	Calabrese et al. 1995	36	
	Triebig et al. 2009	40	50



Reference	Number of workers	Mean duration of exposure (years)	NOAEL ppm	LOAEL ppm	Comments
Hagmar et al. 2000	124–155	12.9–17.9 (range: 2–39)		22	Lifetime weighted average exposure calculated for each worker using historical exposure data Total error score was significantly different from workers in the low exposure group (9 ppm)
Fallas et al. 1993	30	6.5 (range: 1–25)		24.3	Significant differences in the number of subjects with color vials in the red-green or blue-yellow ranges; no significant difference in calculated error scores
Campagna et al. 1996	119	5.3 or 6.8		25	Mathematical threshold of impaired CCI was 4 ppm; the upper limit of the CI was 25.7 ppm
Figueira et al. 1999	57	7.8 (range: 0.3–26.6)	8	63	Significant difference in CCI between age-matched workers and controls. Workers divided into two groups—significant difference in CCI between high-concentration workers (urinary MA level of 1.96 g/L [range: 0.46–3.96 g/L] equivalent to 83 ppm) and age-matched controls. No difference in low-concentration workers (urinary MA levels—mean of 0.02 g/L, range of 0.04–0.41 g/L, equivalent to 8 ppm). CCI scores in low and high exposure groups (CCI in age-matched controls at 1.07/1.11) and 1.02/1.12%)
Seeber et al. 2004a	240	Mean 5–6–6.4			Workers divided into three groups—low, medium, high based on urinary MA and PGA levels. No significant differences in CCI score or visual contrast sensitivity were obtained between groups. No associations were found when workers were divided into groups with long duration–high exposure (an accumulation of 21 ppm-for-over 10 years) and short duration–low exposure. Interpretation of these results is limited by the lack of a control group.





ATSDR Minimal Risk Levels (MRLs) - February 2012

Route	Duration	MRL	Factors	Endpoint	Draft/ Final	Cover Date	CAS Number
STYRENE							
Inh.	Acute	5 ppm	10	Neurol.	Final	11/2010	100-42-5
Inh.	Chr.	0.2 ppm	30	Neurol.	Final	11/2010	100-42-5
Oral	Acute	0.1 mg/kg/day	1000	Neurol.	Final	11/2010	100-42-5

Table 8-1. Regulations, Advisories, and Guidelines Applicable to Styrene

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines			
IARC	Carcinogenicity classification	Group 2B[a]	IARC 2008
WHO	Air quality guidelines		WHO 2000
	TWA based on effects other than cancer or odor/annoyance using an averaging time of 1 week	0.26 mg/m³[b]	
	Based on sensory effects or annoyance reactions, using an averaging time of 30 minutes		
	Detection threshold	0.07 mg/m³[c]	
	Recognition threshold	0.21–8.29 mg/m³[c]	
	Guideline value	0.07 mg/m³[c]	
	Drinking water quality guidelines	0.02 mg/L[d]	WHO 2004

http://www.cdc.gov/niosh/docs/2004-101/calc.htm;
The conversion equation is based on 25 °C and 1 atmosphere

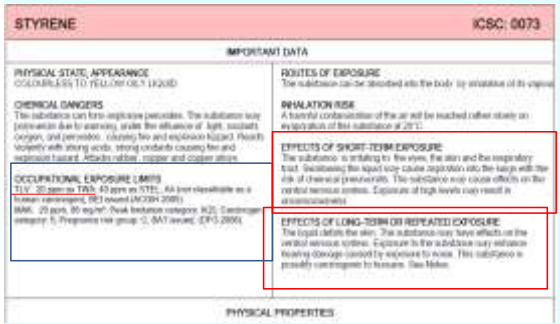
X ppm = (Y mg/m³)(24.45)/(molecular weight)
or
Y mg/m³ = (X ppm)(molecular weight)/24.45

0.061 ppm

STYRENE ICSC: 0073

TYPES OF HAZARD / EXPOSURE	ACUTE HAZARDS / SYMPTOMS	PREVENTION	FIRST AID / FIRE FIGHTING
FIRE	Flammable. Gives off irritating or toxic fumes (or gases) in a fire.	NO open flames, NO sparks, and NO smoking.	Dry powder, Foam, Carbon dioxide.
EXPLOSION	Above 31°C explosive vapour/air mixtures may be formed. See Notes.	Above 31°C use a closed system, ventilation, and explosion-proof electrical equipment.	In case of fire, keep drums, etc., cool by spraying with water.
EXPOSURE		STRICT HYGIENE!	
Inhalation	Dizziness. Drowsiness. Headache. Nausea. Vomiting. Weakness. Unconsciousness.	Ventilation, local exhaust or breathing protection.	Fresh air, rest. Refer for medical attention.
Skin	Redness. Pain.	Protective clothing. Protective gloves.	Remove contaminated clothes. Rinse and then wash skin with water and soap.
Eyes	Redness. Pain.	Safety goggles, or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
Ingestion	Nausea. Vomiting.	Do not eat, drink, or smoke during work.	Rinse mouth. Do NOT induce vomiting. Give plenty of water to drink. Rest.

IPCS WHO UNEP



STYRENE ICSC: 0073

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE
COLOURLESS TO YELLOW OILY LIQUID

CHEMICAL DANGERS
The substance can form explosive peroxides. The substance may polymerize due to exposure to heat, light, oxidant, oxygen, and peroxides. Corrosive to iron and aluminium. Reacts violently with strong acids, strong oxidants causing fire and explosion hazard. Attacks rubber, copper and copper alloys.

OCCUPATIONAL EXPOSURE LIMITS
TLV: 20 ppm as TWA; 40 ppm as STEL; A4 (not classifiable as a human carcinogen) (RD toward LNCSH 2008).
MAK: 20 ppm, 85 mg/m³; Peak limitation category: II(2); Carcinogen category: 5; Pregnancy risk group: C; BAT-value: (EH 5 2000).

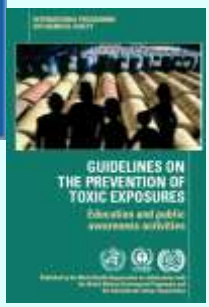
ROUTES OF EXPOSURE
The substance can be absorbed into the body by inhalation of its vapour.

INHALATION RISK
A harmful contamination of the air will be reached rather slowly on evaporation of this substance at 20°C.

EFFECTS OF SHORT-TERM EXPOSURE
The substance is irritating to the eyes, the skin and the respiratory tract. Swallowing the liquid may cause aspiration into the lungs with the risk of chemical pneumonitis. The substance may cause effects on the central nervous system. Exposure at high levels can result in unconsciousness.

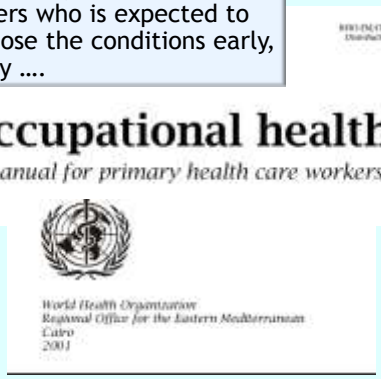
EFFECTS OF LONG-TERM OR REPEATED EXPOSURE
The liquid defats the skin. The substance may have effects on the central nervous system. Exposure to the substance may enhance hearing damage caused by exposure to noise. This substance is possibly carcinogenic to humans. See Notes.

PHYSICAL PROPERTIES



Guidelines are prepared for educating workers, increasing public awareness….
And..

And primary health care workers who is expected to diagnose the conditions early, timely ….



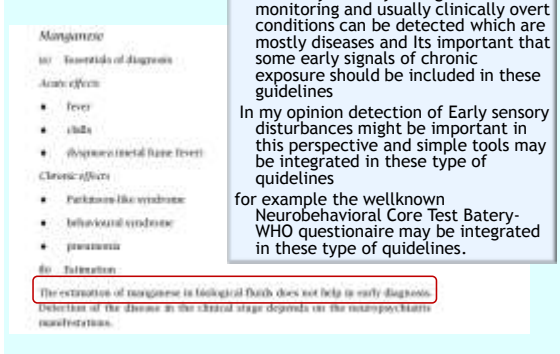
Occupational health

A manual for primary health care workers

World Health Organization
Regional Office for the Eastern Mediterranean
Cairo
2001

5.2 Organic solvents and biological tests used for detection of exposure

Organic solvent and its health effects	Methods of evaluation of exposure
Early detection of occupational diseases: Module 3	29
Trichloroethane	
Acute exposure Mucous membrane and skin irritant. Narcotic. Capable of sensitizing the myocardium to adrenaline thereby causing arrhythmias.	Trichloroethane, trichloroethanol and trichloroacetic acid in expired air, blood and urine.
Chronic exposure Dry, scaly dermatitis.	
Trichloroethylene	
Acute exposure Powerful narcotic, action exacerbated by ethanol. Mild respiratory and skin irritant.	Expired air for trichloroethylene and trichloroacetic acid. Trichloroethanol and trichloroacetic acid in blood or urine.
Chronic exposure Peripheral neuropathy has been reported. Addiction.	



Manganese

(c) Essentials of diagnosis

Acute effects

- fever
- chills
- dyspnoea (metal fume fever)

Chronic effects

- Parkinson-like syndrome
- behavioural syndrome
- pneumonia

(b) Estimation

The estimation of manganese in biological fluids does not help in early diagnosis. Detection of the disease in the clinical stage depends on the neuropsychiatric manifestations.

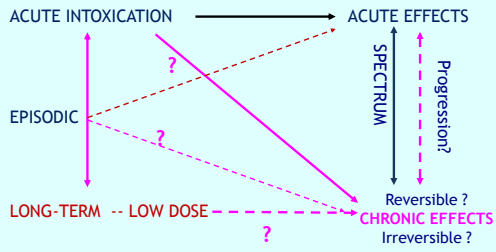
- The investigation of chronic exposure is usually done by biological monitoring and usually clinically overt conditions can be detected which are mostly diseases and Its important that some early signals of chronic exposure should be included in these guidelines

In my opinion detection of Early sensory disturbances might be important in this perspective and simple tools may be integrated in these type of quidelines

for example the wellknown Neurobehavioral Core Test Batery-WHO questionaire may be integrated in these type of quidelines.

NEUROTOXICITY OF CHEMICALS

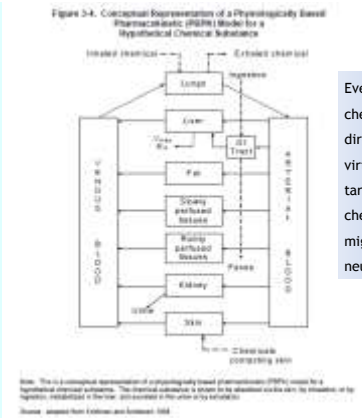
EXPOSURE – EFFECT RELATIONSHIPS



Wellbeing-**Early changes**--subclinical signs-**symptoms**?-clinical illnesses

Exposure-effect relationship

- Acute or chronic
- Features of chemicals (type, danger, toxicologic, metabolism, excretion)
- Age, sex, weight, sensitivity, health status, drug usage, habits
- Working environment (thermal comfort, interactions of physical conditions, climate, pressure, interactions of organizational issues)
- Workplace –occupational health policy, enterprise scale, developing country, work organizational level
- Intake mechanism
  - **inhalation(nasal, mouth), oral(oropharingeal, nasal), cutanous(touch), eye**
- Target organs, health effects
  - irritation, immunologic effect, toxicologic effect- systemic, pheripheric--neurotoxic, carcinogenic, reproductive, hematological, liver, kidney, cardiovascular target organs)



Even though the chemical itself is not directly neurotoxic, in virtue of its effects on target organs any chemical substance might lead to neurotoxic results

Senses on absorption route---

- Touch-dermal exposure
- Smell-inhalation-ingestion exposure
- Taste-inhalation and ingestion exposure
- Eye-eye exposure

Since we gather all information from the environment with our senses, some neurobehavioural disturbances might be reflections of disturbed senses.
Therefore early signs of sensory impairment deserve further systematic evaluation especially for follow up.

Sense

Definition ?

For human ?=? for animal

sensory system

- Vision, sight - ophthalmoception
- Hearing – audioception-vestibular
- Smell - olfactoception
- Taste - gustaception
- Touch - tactioception

Balance-Equilibrioception, acceleration,
Thermoception,
Kinesthetic sence- proprioception,
Nociception,
Other intensive senses

Dimensions ?

Senses have neurobehavioral aspects each of which worth detailed evaluation. Sensory system begins in moleculer level and it leads to series of events which influences our even social life all aspects of this cascade have the potential to affect each other

- Molecular
- Cellular
- Tissue
- Neurological

Complex neuronal interactions

- Neurobehavioral
- Psychosocial
- Social

What do we have?

Questionaires

- Q16 (Hogsted et al 1986)-early disturbances for CNS
- Euroquest symptom questionnaire (Gilioli, 1993; Karlson et al., 2000; Chouaniere et al., 1997; Carter et al., 2002),
  -83 items: chronic effects due to exposure, irritative effects due to acute exposure, personality-related features
- World Health Organization(WHO) sypmtom screening tool(1987) (Anger et al., 2000; World Health Organization,1986)

Test Batteries and computerized system versions

- Neurobehavioral Core Test Battery-Neurobehavioral core test battery NCBT ~40 minutes for screening
- SPES, NES, MANS, AENTB, PENTB, BARS, NESS-2-3,
- BEES- especially epidemiologic repeated aplications;
- NEUTEST

Areas of neurotoxicity assessed with neuropsychological testing

- Prior & Present Health
- Sensory
- Cognitive
- Affect & Mood
- Motor and Tremor
- Effort

Sensory Tests

- Smell--University of Pennsylvania
  Smell Identification Test (UPSIT),Connecticut Chemosensory clinical research center test(CCCRCT), Sniffin'sticks, Elsberg Levy's blast Injection method
- Visual Acuity-- Snellen
- Visual Contrast Sensitivity, Color Vision (Lanthony D15 d)
- Color Vision (Lanthony D15 de saturated panel, Farnsworth-Munsell 100-hue, farnsworth D15, Ishiara plates, standart pseudoisochromatic plates-SPP2, HRR, Velhagen-)
- Visual field (Nagel Anomalascope)

Potential neurophysiological measures of neurotoxicity

Electroretinograms-- Evoked responses from the retina in response to visual stimuli

Flash visual evoked potentials (VEPs)--Cortical response to simple flashes of illumination

Pattern visual evoked potentials (VEPs)--Cortically generated responses elicited by patterns of visual stimuli

Brainstem auditory evoked potentials (BAEPs)-- Responses recorded at or near the cortical surface reflecting volume-conducted electrical activity from brainstem generators in auditory pathway

Middle and late potentials-- Potentials occurring in auditory cortex approximately 10-50 ms after auditory stimulation

"Far-field" somatosensory evoked potentials (SSEPs)--Elicited by electrical stimulation of nerves, producing a large synchronous afferent volley in the CNS

Cortical somatosensory potentials--Recorded from cerebral cortex after presentation of sensory stimuli or direct stimulation of the median nerve

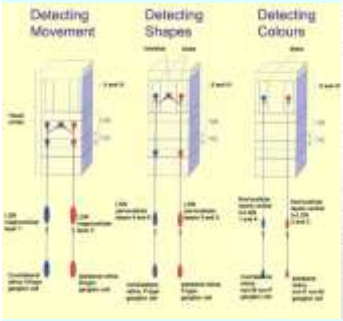
Cerebellar somatosensory potentials--Recorded from cerebellum after stimulation of peripheral nerve such as the ventral caudal tail nerve of rats

vision

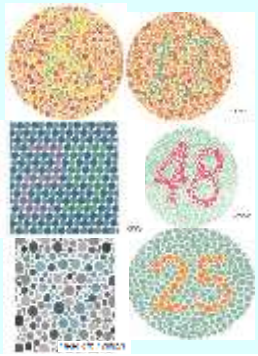
- Molecular — Rodes, cones, retina
- Cellular — photoreseptors; neurotransmitters, optic nerve, frontooccipital,
- Tissue — Cornea lens, iris, fluids,
- Neurological — Eye, eyelid, muscles
- Complex neuronal interactions
- Neurobehavioral — Seeing, bright, detecting colors blue-green-red, signs, Detecting movements, shapes, visual field, night seeing
- Psychosocial
- Social — Disability, Life ---------arts--, sciences, ambiguity...

- 1,3-Butadiene
- 1,4-Dioxane
- 2-Butanone
- Acrolein
- Ammonia
- Carbon Disulfide
- Chlorine
- Chlorine Dioxide & Chlorite
- Dichlorobenzenes
- Ethylene Oxide
- Fluorine, Hydrogen Fluoride, and Fluorides
- Fuel Oils / Kerosene
- Hydrogen Sulfide
- Lead
- Mercury
- Naphthalene, 1-Methylnapthalene, 2-Methylnapthalen
- Nitrophenols
- Stoddard Solvent
- Styrene
- Sulfur Mustard
- White Phosphorus

sight



Color discrimination, arrangements



acquired colour vision losses are frequently tritan, sometimes termed "blue-yellow" loss

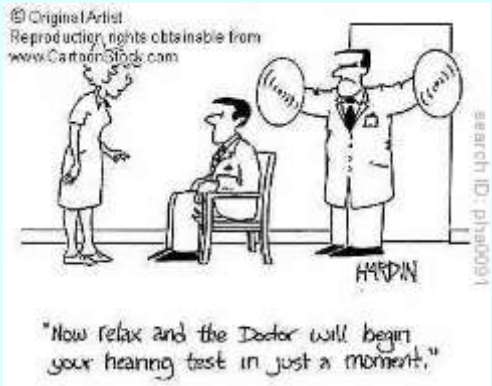
These tritan losses may progress to affect red-green colour vision

Iregren et al summarized tests for color vision in occupational health practice and suggested Lantony d-15 desaturated panel for its sensitivity and simplicity

Contrast sensitivity

Contrast sensitivity loss may reflect long-term cumulative chronic exposure-possibly irreversible damage in neuro-optic pathway.

Inorganic mercury can reduce perception of colour and visual contrast sensitivity and peripheral visual field .
Lead may impair Visual contrast sensitivity-**solvents**, **carbondi-sulfide**, **hegzan**, **perchloroethylene**, **styrene**, **toluene**, **solvent mixtures**, **pesticides** chlorpyrifos color vision and visual contrast sensitivity.
Trichloroethylene, ethyl benzene
Nanoparticles



Hearing

- Molecular
  - Cellular
    - Tissue
      - Neurological
        - Neurobehavioral
          - Psychosocial
            - Social

Neurotransmitters, cilia, haircells, mechanoreceptors,

vestibular nerve, which extends to the vestibular nuclei in the brainstem..

temporal lobe central cortex

Ear:inner-middle-external,

Complex neuronal interactions

Equilibrium organs connection --Fibres from the vestibular nuclei, in turn, extend to cerebellar centres controlling eye movements, and to the spinal cord

Hearing, equilibrium, anxiety, disability

Communicating, understanding, warning signals, employability

Ototoxic substances

Workplace chemicals thought to be ototoxic either on their own or in combination with noise include:

- **Solvents, mixtures** such as butanol, carbon disulphide, ethyl benzene, heptane, n-hexane, styrene, toluene, trichloroethylene and xylene;
- **metals** such as arsenic, lead, manganese, mercury, dimethhlmercury, inorganic mercury and organic tin, cadmium, platinum;
- **pesticides** such as organophosphates and paraquat; and
- **asphyxiants** such as acrylonitrile, carbon monoxide and hydrogen cyanide.

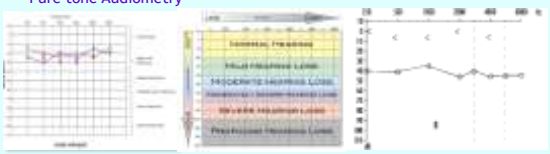
Hearing damage is more likely if exposure is to a combination of substances or to a combination of the substance and noise.

- Medical questionairre

(tinnitus, buzzing, whistling, ringing sound, dizziness, balance, life long history exposure

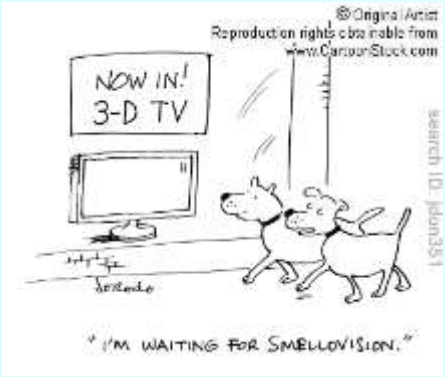
- Clinical examination (Weber, rinne)

- Pure tone Audiometry



Sensoryneural type hearing loss

- Tympanometry, word discrimination tests, evaluation of the attenuation reflex, electrophysical studies (electrocochleogram, Brainstem auditory evoked potentials (BAEPs)-- and radiological studies (routine skull x rays complemented by CAT scan, MRI



Smell

- Molecular
  - Cellular
    - Tissue
      - Neurological
        - Neurobehavioral
          - Psychosocial
            - Social

Olfactory neuro epitelium, mucosa, olfactory nerves,olfactory bulb, olfactory tract

Nose, mouth

Complex neuronal interactions

Personality traits, odour perception, attention, affect, mood

Social preferences, shoping behaviour, Detecting danger, Personality trait? Mate preference

Workplace chemicals reported…

Cadmium,
Chromium,
Nickel
Organic compounds, solvents mixtures,
wood dust,
acrylate, metacrylate,
hydrogen sulfide

Sniff tests-Smell
University of Pennsylvania Smell Identification Test (UPSIT),
Connecticut Chemosensory clinical research center test(CCCRCT),
Sniffin'sticks (EU)
Elsberg Levy's blast Injection method

Olfactometer
- Obtaining olfactory evoked potential (OEP) and electro-olfactograms (EOG)
- Measuring smell thresholds
- Producing expert reports (anosmia)
- Quantitative pain measurement (with CO2), testing analgesics
- Tests with MRI and MEG

Typical gases and liquid substances used in olfactometry:
Odorants (to stimulate the olfactory nerve):
Phenyl ethyl alcohol (PEA) - pleasant stimulant (artificial rose)
Hydrogen sulphide (H2S) - unpleasant stimulant (bad eggs)
- Pain stimulants (to stimulate the trigeminus nerve):
Carbon dioxide - CO2

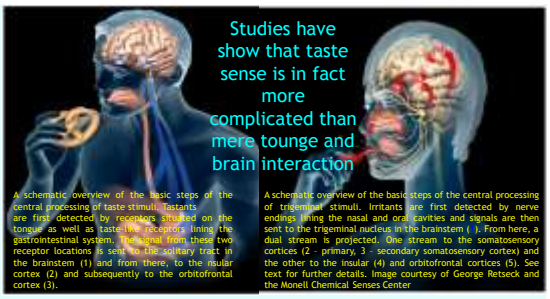
Stimulation response to PEA in a young woman. Test by Professor Dr. Hummel, TU Dresden

Taste

- Molecular — Fugiform papilla, foliat papilla, saliva
- Cellular — Tongue, taste buds, gustatory calyculi, soft palate, pharnx, larynx, uvula, epiglottis, ..
- Tissue — V nerve, VII, IX; X,Thalamus, geniculat ganglion, nucleus solitary tract, glossopharyngeal, mandibular nerve
- Neurological

Complex neuronal interactions

- Neurobehavioral — Flavour; combiantion of smell &taste
- Psychosocial — Sweetness, bitterness, sourness, saltiness,umami, calcium, free fatty ascids
- Social — Dysgeusia, phantageusia, hypo-,ageusia, Nutrition related life conditions

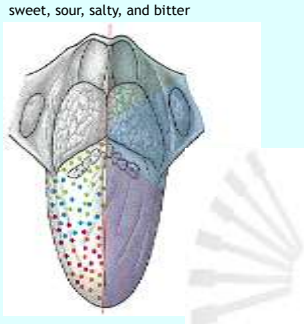


While avaluating any taste-related problems should be asked in detail ...
eg:.Among patients who denied the question "Do you have difficulties in recognizing food or beverages as sweet, sour, bitter, or salty?" no taste disorder was confirmed in 94%. In contrast, the question "Do you have a taste problem?" identified only 10% of the patients with a taste problem.
Furthermore, patients should be questioned with regard to salivation, swallowing, chewing, oral pain, previous ear infections (possibly indicated by hearing or balance problems), oral hygiene, and stomach problems.

Workplace chemicals increase-decrease taste tresholds, disturbances:
- **Organic solvents,**
- **Chromium**
- **Toxic metals - cadmium, lead, mercury, biotoxins**
- **(Panthogosia-absence of stimulus is well known symptom of metal fume fever)**
- **Mercury, cadmium can induce structural alterations in taste buds ?**

Taste Strips"

sweet, sour, salty, and bitter



Gustometer

The picture shows the EEG reading (mean of nine individual measurements) for Cz in reaction to a bitter stimulus. A corresponding stimulation with water showed no potential.

The stimuli used in gustometry are:
- citric acid or hydrochloric acid (sour taste),
- caffeine or quinine hydrochloride (bitter taste),
- sodium chloride (salty taste),
- saccharose (sweet taste),
- monosodium glutamate (umami taste).

Tests using principle of electrical stimulation of the tongue are not suggested

Touch

- Molecular — Merkel cells, nociceptors, immunity(langerhans), melanocytes
- Cellular
- Tissue — Skin, hair follicules, tongue, throat, mucosa
- Neurological — Complex neuronal interactions
- Neurobehavioral — Tactition, anesthesia, paresthesia, tingling, pricking, numbness
- Psychosocial
- Social — absorption, protection, touch, discrimination… chemical, thermal protection

There are also many chemical subtances effecting touch sense and impairment is frequently subclinical

Lead
Elemental mercury
1,1,1 trichloroethane, styrene,
solvent mixtures
n-hexane,toluene, Acrylamide, Organophosphate and other pesticides
Ethylene oxide
Xylene

To identify effects of chemicals these examinations have been studied;

- Vibration perception threshold(VPT),
- two point discrimination,
- dept sense perception,
- temperature treshold,
- pain threshold

Data on comparability methods are limited

Exposure assessment procedure needs:

- workers' monitoring
- working environments' monitoring

Workers' monitoring

Follow health status

Symptoms, behavioral evaluations,

Health exams,

Biologic monitoring,

Chemical, metabolytes-- tissue, body fluids, urine, exaleted breathing air,

Working environment monitoring

Occupational Exposure Limit values .....

MAK, TLV (C), TWA, STEL,

MRLS(ATSDR-2012FEBRUARY)

NOAEL-no observed adverse effect level

LOAEL-lowest observed adverse effect level- 'less serious', 'serious'

AOEL-acceptable operator exposure level

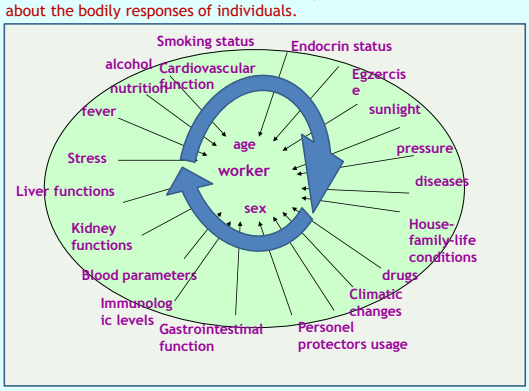
Is biologic and environmental monitoring possible

for chronic exposure

in «real workplaces» and «real world» of developing countries ???

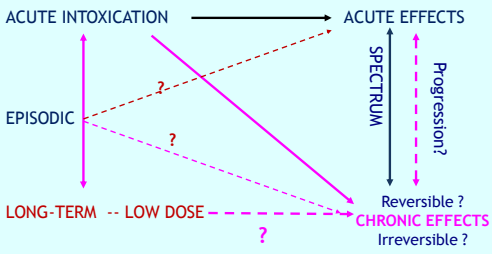
Chronic exposure is a complicated issue even for the developed countries especially when we consider the potential counfounding effect of other environmental factors

Even limit values had been detected and kept we can never be sure about the bodily responses of individuals.



NEUROTOXICITY OF CHEMICALS

EXPOSURE – EFFECT RELATIONSHIPS



Wellbeing-**Early changes**--subclinical signs-**symptoms**?-clinical illness

Developing Countries!

Well recognised –but not well-controlled- neurotoxins:

- Metals, Lead, mercury
- Solvents,
- Pesticides-Organophosphates … others …

"New" generation neurotoxins

- e-waste
- PBDE (Polybrominated diphenyl ether)
- Persistent organic pollutants
- Nanomaterials related…… others …

- Occupational health services
- Poor environmental and biologic monitoring as a survey
- lack of facilities and equipment
- inadequate information systems
- Poor case detection
- Limited resources for research competing causes of ill-health (health services transitions, system, organizational issues)

Control hierarchy

- Identify
- Evaluate
- Control
- Eliminate
- Substitute
- Enclose/separate

Conclusion

- Considerations should be comprehensive -- sensory system impairments might be confounders for neurobehavioral methods
- Might periodic evaluation of all senses together be an early detection tool for chronic exposure ???
- Consensus on standardized questionaires testing sensory perception in detail
  - Not time consuming, simple, but including all traditional senses,
  - Common language for evaluating senses in chronic exposure
- For widespread use and data collection, collaboration with WHO and ILO, and recommendation and training of occupational health teams are needed

Ramazzini's primacy
« Prevention is better than cure »

For prevention we need awareness

which can only be found when it is looked for

Let's look for early signs of sensory disturbances