Work Related Neurological Disorders

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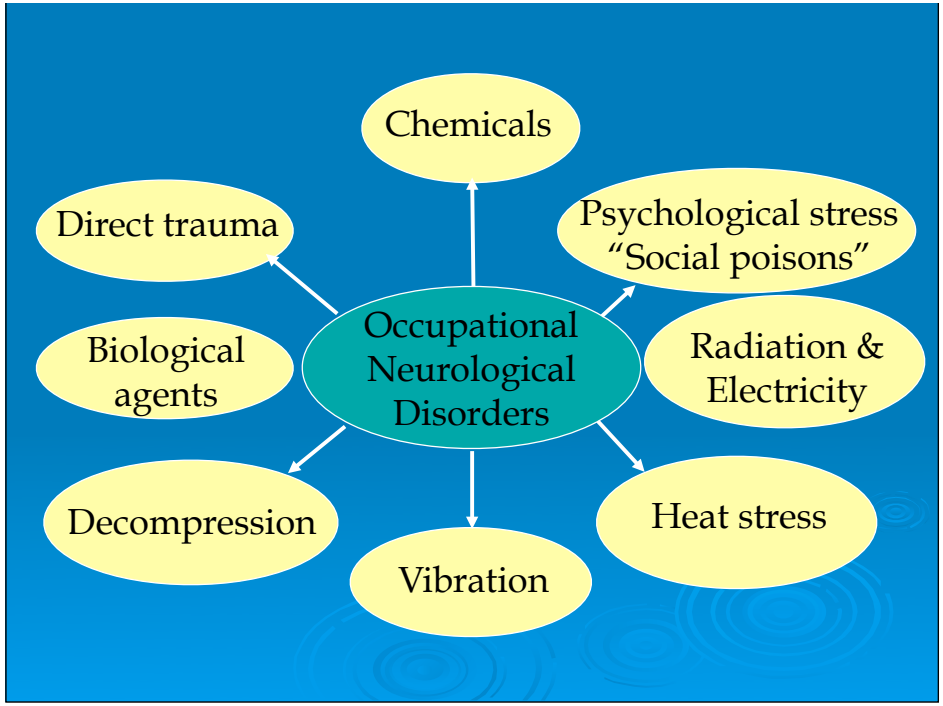
Chemicals
Direct trauma
Psychological stress
"Social poisons"
Occupational
Neurological
Disorders
Biological
agents
Radiation &
Electricity
Decompression
Vibration
Heat stress

Introduction

- CNS particularly susceptible; high metabolic rate
- Heavy metals, solvents and vapours, insecticides, herbicides, fungicides & rodenticides
- Treatment largely symptomatic & supportive
- Recognition of disease potential & prevention of paramount importance

Comprehensive history

- Composition and toxicity rating?
- Single or mixed substances?
- Host dose exposure?
- Detailed job specification?
- Epidemiology - extent of problem? Outbreak?

Additional Considerations

- Exposure may be acute high dose or chronic low dose
- Short or long latency may separate exposure and symptoms
- Pre-existing or coincidental disease may complicate diagnosis
- Symptoms may be numerous and non-specific
- Susceptibility variable; inconsistent correlation with animal toxicity

Additional Considerations

- Damage may be reversible or irreversible
- A cascade of effects may have secondary and systemic complications as well as psychological problems
- Secondary gain complicates diagnosis
- Neurological signs may be absent or subtle within recognised syndromes
- Markers of neurotoxic damage may be normal or non-specific despite signs and symptom
- Must exclude other possible causes - systemic and metabolic disease

Diagnosis

- High index of suspicion
- Recognition of exposure by occupation &specific syndromes
- Elimination of other causes
- Laboratory evaluation*
  - Sampling of water, air or soil
  - Analysis of blood, hair and nails
  - Biochemical markers
  - NCS & EMG (most sensitive), EEG
- Neuroimaging*
- Neuropsychology

*Generally poor sensitivity & specificity

Acute Encephalopathy

- Reversal of sleep pattern
- Headache (raised ICP)
- Irritable, agitation
- Memory impairment
- Confusion
- Epileptic seizures
- Drowsiness
- Coma
- Death

Chronic Encephalopathy

- Dementia - global cognitive decline
- ± superimposed confusion
- ± tremor alone (Mercury)
- ± parkinsonism (Manganese, carbon monoxide)

Peripheral Neuropathy

- Distal paraesthesiae, limb weakness
- Wasting
- Loss of deep tendon reflexes
- Loss of sensation distally
- NCS - axonal sensorimotor pattern of peripheral neuropathy; secondary demyelination

Delayed Effects

- Organophosphates - delayed neuropathy
- CO - delayed neuropsychiatric syndrome
- Pesticides - delayed PD & dementia

Lead Toxicity

- Acute - children; chronic - adults
- Solder, lead shot, insecticides, auto body shop, storage battery manufacture, smelter, paint, water pipes, gasoline
- Syndromes (adults) based on long-term serum levels:
  - 25-60 μg/dL - irritability, headache, myalgia, anorexia, abdominal pain
  - > 60 μg/dL - peripheral neuropathy (wrist/foot drop)
- Differential diagnosis - renal colic, AIP, vasculitis

Lead Toxicity

- Diagnosis:
  - Whole blood Pb concentrations
    - N < 5 µg/dL
    - Safe < 30 µg/dL
    - Needs close monitoring > 40 µg/dL
  - Urine lead levels (N < 150 µg/dL)
  - Blood zinc protoporphyrin > 100 µg/dL
  - Urinary aminolevulinic acid > 15 mg/L
  - Low activity of aminolevulinic acid dehydratase, coproporphyrinogen oxidase & ferrochetalase
  - FBP - anaemia with basophilic stippling of RBC
  - NCS - small APs, slow NCV

Lead Toxicity - Treatment

- Decontamination
- Supportive care
  - Reduction of ICP - dexamethasone, mannitol
  - Nursing care, analgaesia, physio & OT
- Judicious use of chelating agents (> 40 µg/dL)
  - Calcium disodium edetate or calcium EDTA at 30 mg/kg every 24h, OR
  - Dimercaprol (British anti-Lewisite [BAL]) single 4-5 mg/kg deep i.m., OR
  - meso-2,3-dimercaptosuccinic acid (DMSA or succimer)

Mercury Toxicity

- Thermometers, other gauges, dental clinic (amalgams), felt hat manufacture ("mad hatter syndrome), electroplating, photography
- 10,000 tons of mercury mined per year
- 2,000-3,000 tons of mercury released into atmosphere annually; runoff into natural bodies of water
- Minamata (Bay) disease - outbreak in Japan affecting 2,500 people through ingestion of fish contaminated by methyl mercury
- Elemental vs. Organic (methyl, ethyl) mercury

ELEMENTAL Mercury Toxicity

- Acute
  - Encephalopathy
- Chronic
  - Sensorimotor peripheral neuropathy
  - Parkinsonism
  - Dysarthria

Minamata Disease

Mehtyl Mercury

- Cerebral cortex - encephalopathy, erethism (abnromal sensitivity to stimulation of any type), visual field constriction, spasticity, dementia
- Cerebellum - tremor, dysarthria, ataxia
- Peripheral nerves - paraesthesiae of hands, feet and mouth
- Teratogenicity - microcephaly, micrognathia, mental retardation, blindness, motor deficits

Mercury Toxicity

- Diagnosis:
  - Blood Hg concentrations
    - N < 10-20 μg/L
  - Urine Hg levels
    - N < 20 μg/L
  - NCS - small APs, slow NCV

Mercury Toxicity - Treatment

- Decontamination
- Supportive care
- Judicious use of chelating agents
  - Dimercaprol (BAL) i.m. 3-5 mg/kg q4h on day 1, q12h on day 2, then od x 3/7, 2-day interruption, OR
  - 2,3-dimercapto-propane-1-sulfonate (water soluble form of BAL), OR
  - meso-2,3-dimercaptosuccinic acid (DMSA or succimer)
- Prevention
  - Monitoring high risk occupations
  - Adequate ventilation
  - Avoid vacuuming of spilled mercury
  - Removal or workers with levels > 50 µg/L

Arsenic Toxicity

- Pesticides, pigments, paint, electroplating, smelter, semiconductors
- Encephalopathy & peripheral neuropathy
- Carcinogenesis
- Tens of millions of people in Bangladesh at risk
  - contaminated drinking (well) water
  - natural geologic sources leaching into aquifers
  - Mining

Acute Arsenic Poisoning

(ingestion)

- Multisystem disaster
  - GI - vomiting, bloody diarrhoea
  - MSK - rhabdomyolysis
  - Renal - myoglobinuric renal failure
  - CVS - arrhythmias, hypotension
  - CNS - seizures, coma - death
- Survivors
  - Mees lines, PN (D7-14)
  - ± Impaired cognition
  - Slow & incomplete recovery over years

Arsenic Inhalation

- Acute
  - Encephalopathy
- Chronic
  - Vasculopathy, gangrene ("Blackfoot disease")
  - Less severe peripheral neuropathy

Arsenic Toxicity

- Diagnosis
  - Urinary arsenic > 70 μg/dL
  - NCS
- Treatment
  - BAL > penicillamine
  - Acute hemodialysis

Other Heavy Metals

Agent	Occupational/other exposure	Acute	Chronic
Manganese	Iron industry, welding, mining, smelter, fireworks, fertilizer, dry cell batteries	Encephalo-pathy	Pakinsonism
Tin	Canning industry, solder, electronics, plastics, fungicides	Delirium	Encephalo-myelopathy

Solvents

Agent	Occupational/other exposure	Acute	Chronic
Carbon disulfide	Rayon manufacture, preservatives, textiles, rubber cement, varnish, electroplating	Encephalo-pathy	Pakinsonism, neuropathy
Trichlorethylene	Paint, degreasers, spot removers, decaffeination, dry cleaning, rubber solvents	Narcosis	Encephalo-pathy, trigeminal neuropathy

Solvents

Agent	Occupational/other exposure	Acute	Chronic
Hexacarbons (*n*-hexane, methyl-*n*-butyl ketone or MNBK)	Paints, paint removers, varnish, degreasers, rapid-drying ink, glues, cleaning agents, glues for making shoes in poorly vented cottage industry, MNBK in plastics	Narcosis	Neuropathy, encephalo-pathy, ataxia

Insecticides

Agent	Occupational/other exposure	Acute	Chronic
Organophos-phates, carbamates	Manufacture & application (agriculture)	Cholinergic crisis	Ataxia, neuropathy, myelopathy
Carbon monoxide	Accidental or deliberate exposure to motor vehicles, faulty gasoline-fuelled heaters	Anoxic encephalo-pathy	Dementia, delayed neuropsychia-tric syndrome, cerebellar dysfunction Parkinsonism

3 Stages of Organophosphate Toxicity

- Acute cholinergic crisis (immediate)
  - Nicotinic effects - limb weakness, fasciculation, tachycardia
  - Muscarinic effects - lacrimation, salivation, miosis, sweating, abdominal cramps
- Intermediate syndrome (D2-4)
  - Profound weakness of facial, neck and proximal limb & respiratory muscles
  - Generalised areflexia
  - DDx - GBS, MG, periodic paralysis
- Organophosphate-induced delayed neuropathy (W1-5)
  - motor > sensory(survivors may develop UMN signs mimicking MND)

Organophosphate Toxicity - Mx

- Diagnosis
  - Levels of compound or metabolites in blood or urine
  - RBC/plasma cholinesterase levels
- Decontamination
  - If splashed, discard clothing & wash skin thoroughly
  - Gastric lavage if ingested
- Supportive care
  - ABCs of emergency, continuous ECG monitoring
  - s/c atropine 0.5-1 mg every 15' until pupils dilated, flushed face, dry mouth and dry skin
  - i/v atropine 2 mg q2h to suppress airway secretions
- Oxime therapy
  - Continuous ivi of pralidoxime chloride (to reactivate acetylcholinesterase)

Conclusion

- Many syndromes can be eliminated if care were taken to protect the environment
- Neurotoxins are one of the greatest mimickers of neurological disease
- High index of suspicion is essential
- Recognition of specific syndromes & prevention are of paramount importance