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اسم المادة باللغة العربية: السموم العامة

اسم المادة باللغة الإنكليزية: **General toxicology**

المرحلة: الرابعة

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عنوان المحاضرة باللغة العربية: الاستجابة السمية للجهاز العصبي.

عنوان المحاضرة باللغة الإنكليزية:**Toxic Responses of the Nervous System**

Toxic Responses of the Nervous System

Efforts to understand the mechanism of action of individual neurotoxic compounds have begun with the identification of the cellular target.

In the NS, this has most often been one of four targets: the neuron, the axon, the myelinating cell, or the neurotransmitter system, neurotoxic compounds may be identified which cause:

-neuronopathies
-axonopathies
- myelinopathies

- neurotransmitter-associated toxicity

neuronopathies

myelinopathies

axonopathies

neurotransmitter-associated toxicity

Neuronopathies

Certain toxicants are specific for neurons, or sometimes a particular group of neurons, resulting in their injury or, when intoxication is severe enough, their death.

Some of the unique features of the neuron include a high metabolic rate, a long cellular process that is supported by the cell body, and an excitable membrane that is rapidly depolarized and repolarized.

Methyl Mercury

There are two tragically poisoning for methyl mercury was occur in in Japan and Iraq

The residents of Minamata Bay in Japan, whose diet was largely composed of fish from the bay, were exposed to massive amounts of MeHg when mercury-laden industrial effluent was rerouted into the bay

MeHg injured even more people in Iraq, with more than 400 deaths and 6000 people hospitalized. In this epidemic, as well as in several smaller ones, the effects occurred after the consumption of grain that had been dusted with MeHg as an inexpensive pesticide

The clinical picture of MeHg poisoning varies with both the severity of exposure and the age of the individual at the time of exposure.

In adults, the most dramatic sites of injury are the neurons of the visual cortex and the small internal granular cell neurons of the cerebellar cortex, whose massive degeneration results in blindness and marked ataxia.

In children, developmental disabilities, retardation, and cognitive deficits occur.

The mechanism of MeHg toxicity has been the subject of intense investigation. However, it remains unknown whether the ultimate toxicant is MeHg or the liberated mercuric ion.

Although Hg2+ is known to bind strongly to sulfhydryl groups, it is not clear that MeHg results in cell death through sulfhydryl binding.

Axonopathies

The neurotoxic disorders termed axonopathies are those in which the primary site of toxicity is the axon itself.

Axonopathies can be considered to result from a chemical transection of the axon.

Furthermore, as these axons degenerate, the result is most often the clinical condition of peripheral neuropathy, in which sensations and motor strength are first impaired in the most distal extent of the axonal processes, the feet and hands gamma-Diketones Carbon

Disulfide

Pyridinethione

This compound is a chelating agent that is usually encountered as the zinc complex.

ZPT is a biocide that has antibacterial and antifungal properties.

It is the active ingredient in shampoos and other preparations for the treatment of seborrheic dermatitis and dandruff.

ZPT is also used as an antifouling agent for ship paints, drywall, and tarps, and as an antibacterial agent for incorporation into cleaning sponges.

Myelinopathies

Toxicants exist that result in the separation of the myelin lamellae, termed intramyelinic edema, and in the selective loss of myelin, termed demyelination.

Remyelination in the CNS occurs to only a limited extent after demyelination. However, Schwann cells in the PNS are capable of remyelinating the axon after a demyelinating injury.

Lead

Lead exposure in animals result in a peripheral neuropathy with prominent segmental demyelination.

adults are exposed to lead in occupational settings through lead smelting processes and soldering and in domestic settings through lead pipes or through the consumption of "moonshine" contaminated with lead.

Children, especially those below five years of age, have higher blood levels of lead than adults in the same environment, due to the mouthing of objects and the consumption of substances other than food.

In addition, children absorb lead more readily, and the very young do not have the protection of the blood–brain barrier.

In young children, acute massive exposures to lead result in severe cerebral edema, perhaps from damage to endothelial cells.

Children seem to be more susceptible to this lead encephalopathy than adults

Astrocytes

astrocytes are now known to perform and regulate a wide range of physiological functions in the CNS.

Indeed, the astrocyte appears to be a primary means of defense in the CNS following exposure to neurotoxicants, as a spatial buffering system for osmotically active ions and as a depot for the sequestration and metabolic processing of endogenous molecules and xenobiotics.

Ammonia

Hepatic encephalopathy (HE) and congenital and acquired hyperammonemia lead to excessive brain ammonia (ammonium, $NH4^+$) accumulation. The condition results from liver failure.

At high CNS concentrations ammonia produces seizures, resulting from its depolarizing action on cell membranes,

whereas, at lower concentrations, ammonia produces stupor and coma, consistent with its hyperpolarizing effects.

GS
Glutamate + ATP + NH_3 ----------→ Glutamine + ADP + phosphate

Methionine Sulfoximine

Methionine sulfoximine (MSO) is an irreversible inhibitor of the astrocyte-specific enzyme, GS. Ingestion of large amounts of MSO leads to neuronal cell loss. MSO also leads to large increases of glycogen level.