ARE WE SLOWLY POISONING OURSELVES? EATING HERBICIDES AND PESTICIDES WITH GM AND OTHER FOODS

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MEDCINAL CHEMISTRY AND DRUG DESIGN
Chemistry, Pharmacology, Physiology, Biochemistry, Toxicology,Drug Design, Receptors, Enzymes

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GM CROPS DO WE NEED THEM? ARE THEY SAFE?
MAY 10th 2003

WHAT ARE WE TALKING ABOUT?

HERBICIDES AND PESTICIDES THAT ARE CLOSELY RELATED ORGANIC COMPOUNDS OF PHOSPHORUS

1.ORGANOPHOSPHONATES

- **NERVE AGENTS- eg. SARIN, SOMAN etc.**
- **BIS PHOSPHONATES - OSTEOPOROSIS- BONE**
- **HERBICIDES- GLYOPHOSATE, GLUFOSINATE**

2. ORGANOPHOSPHATES, OPs

- **PESTICIDES - eg MALATHION, PARATHION, DIAZINON etc.**

CONVERTED IN LIVER TO ACTIVE COMPOUNDS

- **RESEARCH COMPOUNDS eg DFP**

BIG PROBLEM - INNUMERABLE PROCESSES IN THE BODY INVOLVE PHOSPHATE GROUPS- AS ON/OFF SWITCHES. GENE ACTIVATION, GLUCOSE TRANSPORT, HORMONE RESPONSE, ENERGY PRODUCTION. ALL CAN BE POTENTIALLY DAMAGED

DESIGNING DRUGS, HERBICIDES, PESTICIDES

PRINCIPLES

DRUGS - HIGHLY SPECIFIC/UNIQUE TARGET eg. BACTERIAL CELL WALL- PENICILLINS OR DISCRIMINATING INTERACTION WITH TARGET TISSUE/SYSTEM eg SSRIs- DEPRESSION

HERBICIDES - UNIVERSAL TARGET IN WEEDS

PESTICIDES - UNIVERSAL TARGET IN INSECTS, PESTS (aphids, fungi, etc)

ALWAYS THE UNEXPECTED-

PENICLLINS PROVOKE ALLERGIC REACTIONS

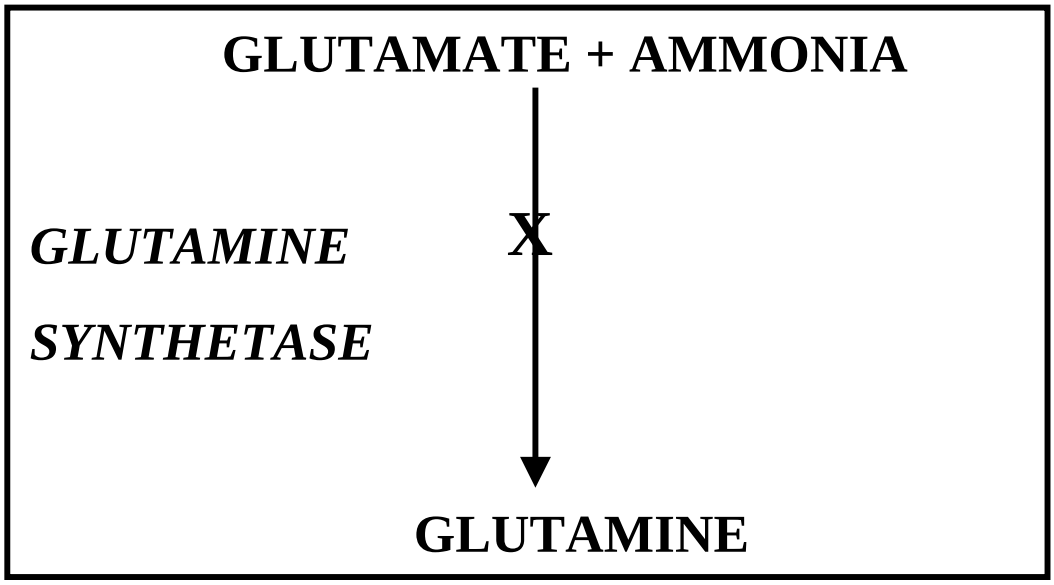
LACK OF DISCRIMINATION BETWEEN GOOD AND BAD PLANTS, PESTS, ORGANISMS -ESPECIALLY MAN

FOMULATION OF ACTIVE COMPOUND CAN INTRODUCE NEW PROBLEMS

SOD'S LAW PREVAILS - SIDE EFFECTS, WARNINGS, ABANDONMENT/WITHDRAWAL - "BIG BUCKS"

GLUFOSINATE AMMONIUM

TARGET- INHIBITION OF GLUTAMINE SYNTHETASE



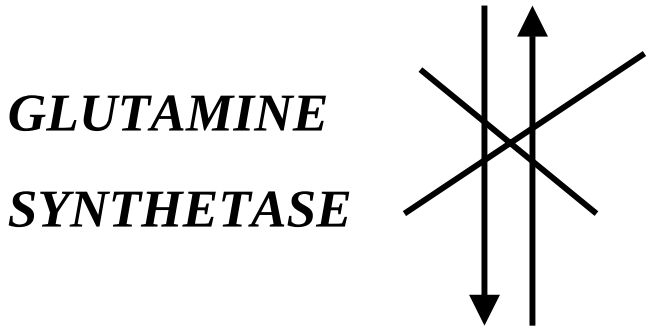
RATIONALE - AMMONIA IS HIGHLY TOXIC TO PLANTS- BLOCK THIS PATHWAY TO KILL WEEDS

BIG PROBLEM - THIS PATHWAY IS UNIVERSAL- MAN, INSECTS, MICRO-ORGANISMS- EVERYWHERE

IN MAN/MAMMALS AMMONIA IS TOXIC BUT MOST IS REMOVED BY ANOTHER PATHWAY

IN MAN

GLUTAMATE + AMMONIA



GLUTAMINE

GLUTAMINE MAINTAINS HOMEOSTATIC BALANCE ESPECIALLY IN BRAIN, IMMUNE SYSTEM AND GUT

MOST ABUNDANT FREE AMINO ACID IN BODY 50-60% OF TOTAL; 20% PLASMA POOL, READILY CROSSES BBB- 10-15 x HIGHER IN BRAIN THAN BLOOD

GUT UTILISES 40% OF BODY'S GLN- ALSO MAJOR FUEL FOR BRAIN, IMMUNE CELLS,KIDNEYS LIVER

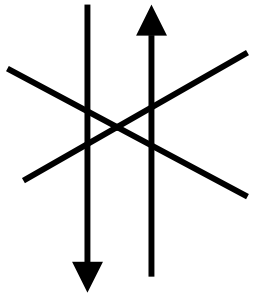
PRODUCTION - SKELETAL MUSCLE FOLLOWED BY LIVER, LUNGS, BRAIN

THERE IS MORE !!

GLUTAMATE + AMMONIA

GLUTAMINE

SYNTHETASE



GLUTAMINE

DETOXIFICATION

INCREASES RESISTANCE TO INFECTION

REGULATION OF GLUCOSE METABOLISM

KEY ROLE NUCLEIC ACID SYNTHESIS

ANABOLIC- PROTEIN IN SKELETAL MUSCLE

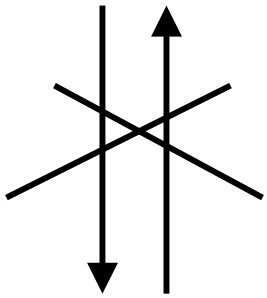
PROTECTS AGAINST BURNS, TRAUMA, ILLNESS

DAMS ARE TROUBLE - LOOK BEHIND

GLUTAMATE + AMMONIA

GLUTAMINE

SYNTHETASE



GLUTAMINE

<u>GLUTAMATE</u> PLAYS A KEY ROLE- MAN/MAMMALS

PREMIER EXCITATORY NEUROTRANSMITTER

DEVELOPMENT OF FOETAL BRAIN

IMPORTANT IN MEMORY AND LEARNING

EXCITATORY TRANSMITTER IN GUT- ENTERIC NERVOUS SYSTEM - APOPTOSIS, CELL DEATH

SOURCE OF GABA- INHIBITORY TRANSMITTER IN GUT AND BRAIN

CONCLUSION - 1

IT IS DIFFICULT TO CONCEIVE OF A MORE POTENTIALLY DAMAGING TARGET FOR COMPOUNDS DESTRUCTIVE TO HUMAN HEALTH AND WELL-BEING THAN THE

GLUTAMATE-GLUTAMINE-GLUTAMINE SYNTETHASE SYSTEM

ANY DISRUPTION OF THIS FINELY BALANCED AND ESSENTIAL SYSTEM BY COMPOUNDS SUCH AS GLUFOSINATE WILL HAVE FAR-REACHING AND LONG-TERM CONSEQUENCES

EVIDENCE - 1?

HUMANS

ACUTE HIGH DOSAGE- SWALLOWED
SUICIDE ATTEMPTS, ACCIDENTS

NEUROTOXICITY **- CONVULSIONS,
MENTAL DISTURBANCE MEMORY LOSS

3-METHYLPHOSPHINYLPROPIONIC ACID
MAJOR METABOLITE - ALSO NEUROTOXIC

CONGENTIAL MALFORMATIONS ** -
Odds Ratio 2.45 (95% CI 7.70-0.78)

EXTEND, FOLLOW UP - DO NOT DISMISS

RESPIRATORY FAILURE, APNOEA

SURFACTANT IN FORMULATION CARDIO-TOXIC

ULTRA HIGH DOSES NOT RELEVANT TO TOXIC
EFFECTS ASSOCIATED WITH PROPER USAGE

DRUG INDUSTRY USES THIS KIND OF EVIDENCE, IF AVAILABLE, TO STOP OR CHANGE PROJECT DIRECTION

LABORATORY ANIMALS - MICE

CONVULSIONS - STIMULATION OF GLUTAMATE RECEPTORS (NMDA)- cf. LAMOTRIGINE

NITRIC OXIDE RELEASE - WIDESPREAD-BLOOD PRESSURE, BRAIN IMMUNE SYSTEM, RADICAL

EMBRYO CULTURE CELLS- APOPTOSIS OF NEUROEPITHELIAL CELLS-TERATOGENIC

<u>SINGLE EXPOSURE</u> OF PREGNANT MICE AT TIME OF HIPPOCAMPAL NEUROGENESIS IN FOETUS LEAD TO BRAIN FUNCTIONAL ABNORMALITIES- GWVs

MORTALITY INCREASED WHEN EXPOSURE OCCURRED IN DAYLIGHT- WHEN APPLIED!

ALL IN AGREEMENT WITH HUMAN DATA AND EXTENDS IT

INSECTS, FISH, SOIL BACTERIA/FUNGI

BUTTERFLIES- SKIPPER MOULT- GENERAL

CLAM & OYSTER LARVAE

SOME FISH ESPECIALLY RAINBOW TROUT

BENEFICIAL PREDATORY INSECTS MORE AFFECTED THAN PESTS THEY PROTECT AGAINST

INHIBITION OF BENEFICIAL SOIL BACTERIA (40%) AND FUNGI (20%)

NITROGEN FIXING BACTERIA RHIZOBIAL NODULATION REDUCED

CELLULOSE DECOMPOSITION DOWN 78% AT 150 ppm

PLANT PATHOGENS MORE RESISTANT THAN ANTAGONISTIC ORGANISMS

KNOCK ON TO BIRD LIFE ?

DO WE REALLY WANT THIS STUFF?

FOOD

WHO/FAO ADI 0.02 mg/kg - 20 ppb = 1.4 mg/70 kg MAN

APPLE SPRAYS - 540 ppm

PREHARVEST DESSICANT! ADDS TO OVERALL LOAD

PEAS 3 ppm 3 mg/kg

WHEAT 1 ppm

POTATOES 0.1 mg/kg plus 2.4 mg/kg 3-MMPA

FLOUR 10-100% WHEAT RESIDUES

BRAN 10-600% BRAN

BARLEY STRAW & PEA STALKS (50 mg/kg)

WHEAT STRAW FIELD BEAN STALKS (20 mg/kg)

HUMAN HAZARDS: POTATOES, PEAS, [LIVER & KIDNEY]FROM ANIMALS FED ON CONTAMINATED CEREAL STRAW

OTHER RESIDUES NOT CONSIDERED eg OPs

WATER

EPA - PERSISTENT AND MOBILE CONTAMINANT

PERSISTS IN SOILS FROM 3- 42 DAYS DEPENDING ON NATURE-eg SANDY vs CLAY

3-MPPA LEACHED OUT 20 x FASTER

QUESTIONS

1. EFFECT ON GUT ORGANISMS?

2. EFFECT ON ORGANISMS AT SEWAGE TREATMENT WORKS?

COMMERCE WINNING OUT OVER SCIENCE IN CONSIDERATION OF HAZARDS

BIG GAPS NEED FILLING

GLYPHOSATE (ISOPROPYLAMMONIUM) etc

TARGET - INHIBITION OF FORMATION OF 5-ENOLPYRUVYLSHIKIMATE-3-PHOSPHATE, EPSP,

SHIKIMATE-3-PHOSPHATE + PHOSPHOENOL PYRUVATE (PEP)

5-ENOLPRUVYL-3-PHOSPHATE

SHIKIMATE-CHORISMATE PATHWAY -ESSENTIAL AROMATIC AMINO ACIDS TRP, TYR, PHE

THIS PATHWAY IS NOT PRESENT IN HUMANS

IT IS PRESENT IN SOME OTHER ORGANISMS

PEP IS WIDELY INVOLVED IN MANY OTHER BIOCHEMICAL REACTIONS IN HUMANS

PHOSPHOENOLPYRUVATE IN HUMANS

GANGLIOSIDE SYNTHESIS - KEY MEMBRANE COMPONENTS ESPECIALLY IN BRAIN/NERVES. ALSO LIVER, SPLEEN, RBCs

GLYCOLYSIS (ALL CELLS) - BREAK DOWN OF SUGAR TO PROVIDE ENERGY

GLUCONEOGENESIS (LIVER, KIDNE) - INVOLVING SYNTHESISING GLUCOSE FROM NON-SUGAR PRECURSORS ESPECIALLY IMPORTANT FOR BRAIN AT TIME OF STARVATION.

OH YES! FORMULATION-

SURFACTANT(S) AND SOME OTHER COMPONENTS (DIOXANE) ARE ALSO TOXIC

TOXICITY

DEPENDS ON ROUTE OF ADMINISTRATION

MOST TESTING HAS USED ONLY ORAL ROUTE -INHALATION MOST SERIOUS, DERMAL ALSO IMPORTANT

LETHAL - SUICIDE ATTEMPTS 10-20% SUCCESSFUL WITH AS LITTLE AS 100 ml [ACUTE TOXICITY VERY LOW]

SEVERE NEUROTOXICITY - 12 YEAR OLD IN CANAL WITH 4 x RECOMMENDED AMOUINT OF ROUNDUP- COMPLETE PARALYSIS FOLLOWED BY ONLY PARTIAL RECOVERY AFTER 5 YEAR

ONE MAN DEVELOPED PARKINSON'S DISEASE AFTER ONE ACCIDENTAL EXPOSURE

ORIGINAL NEUROTOXICITY TESTS OF MONSANTO RULED INVALID BY EPA !!

WIDESPREAD DISTURBANCES OF MANY BODY SYSTEMS REPORTED AFTER EXPOSURES AT NORMAL USE LEVELS

GLYPHOSATE IS MOST FREQUENT CAUSE OF COMPLAINTS AND POISONING IN UK (PESTICIDES TRUST 1996)

MOST COMMON SYMPTOMS

SEVERE CENTRAL, AUTONOMIC AND PERIPHERAL NEUROLOGICAL EFFECTS

BALANCE DISORDER, VERTIGO

REDUCED COGNITIVE CAPACITY

SEIZURES

VISION, SMELL, HEARING, TASTE

HEADACHES, SPACINESS

DROPS IN BLOOD PRESSURE

BODY-WIDE TWITCHES AND TICS

MUSCLE PARALYSIS

PERIPHERAL NEUROPATHY

LOSS OF GROSS AND FINE MOTOR SKILLS

EXCESSIVE SWEATING

SEVERE FATIGUE

ENDOCRINE DISORDERS-

STEROIDOGENESIS INHIBITED GENE SUPPRESSION?

ADRENAL DEFICITS

OESTROGEN A FACTOR IN SENSITISATION- β–GLUCURONIDASE?

SEVERE DIGESTIVE PROBLEMS AFTER OVER EXPOSURE

NAUSEA

DIARRHOEA

DEPRESSION OF LIVER DETOXIFYING ENZYMES (INTERACTION WITH SOME DRUGS- CIMETIDINE)

BRONCHIAL CONSTRICTION, PLEURITIC CHEST PAIN, NASAL CONGESTION

SWELLING OF ARMS, LEGS, FACE, ABDOMEN

RBCs - MIS-SHAPEN, IMPAIRED, HAEMOLYSIS -POEA

THESE SYMPTOMS ARE SIMILAR TO THOSE REPORTED IN A NUMBER OF OVERLAPPING SYNDROMES

GWS, MCS, ME-CFS, PESTICIDE POISONING, FMS

SYMPTOMS	OPs	GWS	MCS	FMS	CFIDS	MS	AIDS
JOINT PAIN	+	+	+	around joint area	+	+	+
FATIGUE	+	+	+	+	+	+	+
HEADACHE	+	+	+	+	+	+	+
MEMORY PROBLEMS	+	+	+	+	+	+	+
SLEEP DISTURBED	+	+	+	+	+	?? due to medicines	+
SKIN PROBLEMS	+	+	+	+	+	burning skin	+
PROBLEMS CONCENTR^{N}	+	+	+	+	+	+	+
DEPRESSION	+	+	+	+	+	+	+
MUSCLE PAIN	+	+	+	+	+	+	+
DIZZINESS	+	+	+	+	+	+	+
G.I. - Irr. Bow.	+	+	+	+	+	+	+
PERIPH PARESTHES/ TINGLING	+	+	+	+	+	+	+
CHEM/ENVIR SENSITIVITY	+	+	+	+	+	Reported	_
EYE PROBLEMS	+	+	+	+	+	+	+
ANXIETY	+	+	+	+	+	+	+
TACHY&/OR CHEST PAIN	+	+	+	+	+	+	+
BREATHING PROBLEMS	+	+	+	Reported	+	+	+
LIGHT SENSITIVITY	+/-	+	+	Reported	+	+	_

+ Literature. Reported = Anecdotal **Adapted from Jackie Burkhead**

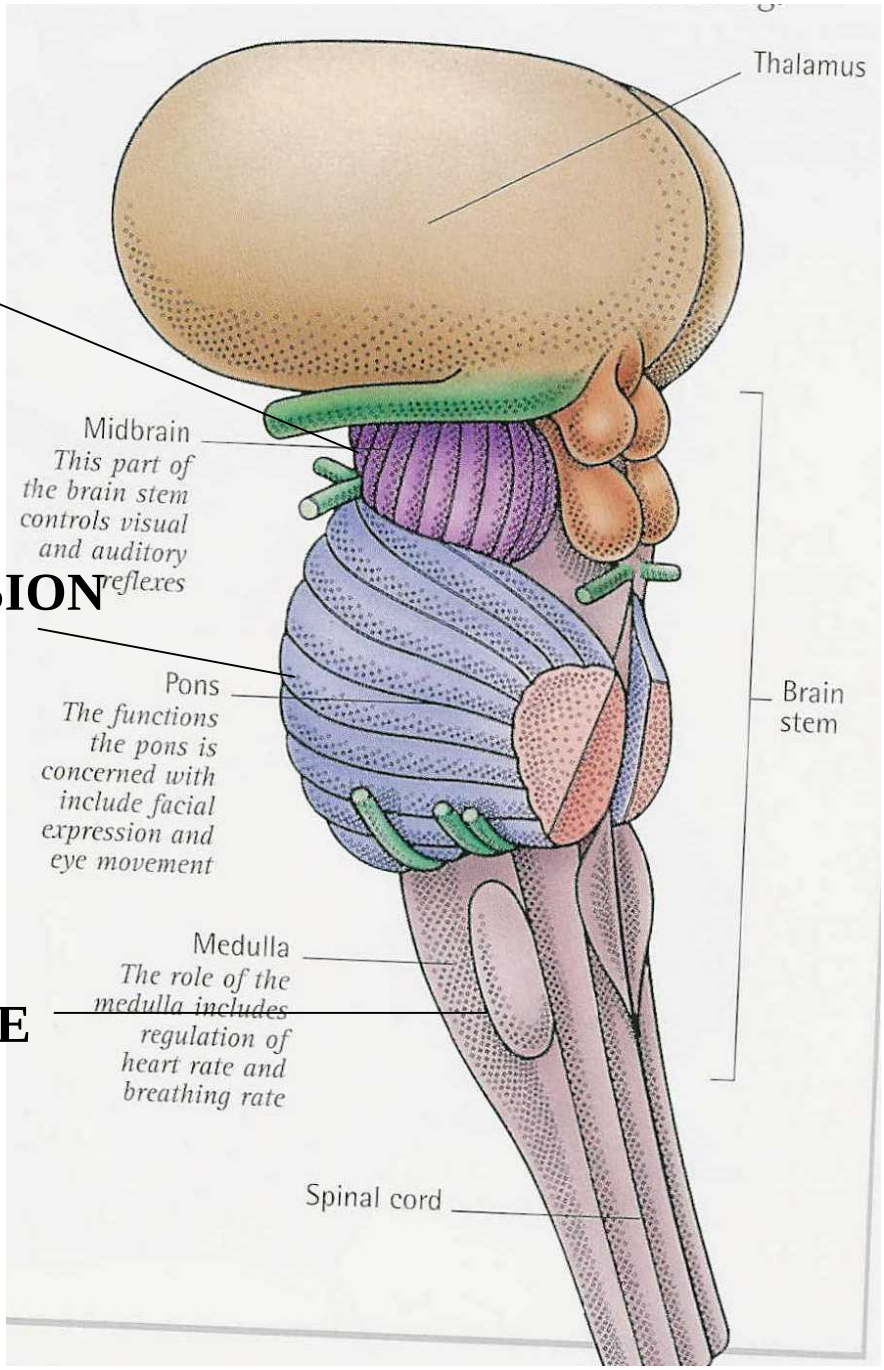
INFORMATION CENTRES- THALAMUS relay station for SENSORY NERVES BRAIN STEM, SPINAL CORD TO CEREBRUM-PAIN

BRAIN STEM REGULATES VITAL FUNCTIONS- HEART BEAT, RESPIRATION, BLOOD PRRESSURE, DIGESTION, SWALLOWING, VOMITING etc

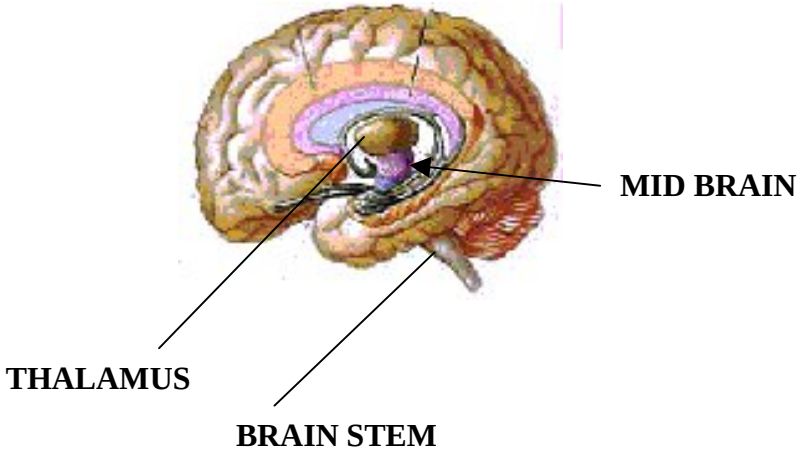
VISUAL
AUDITORY

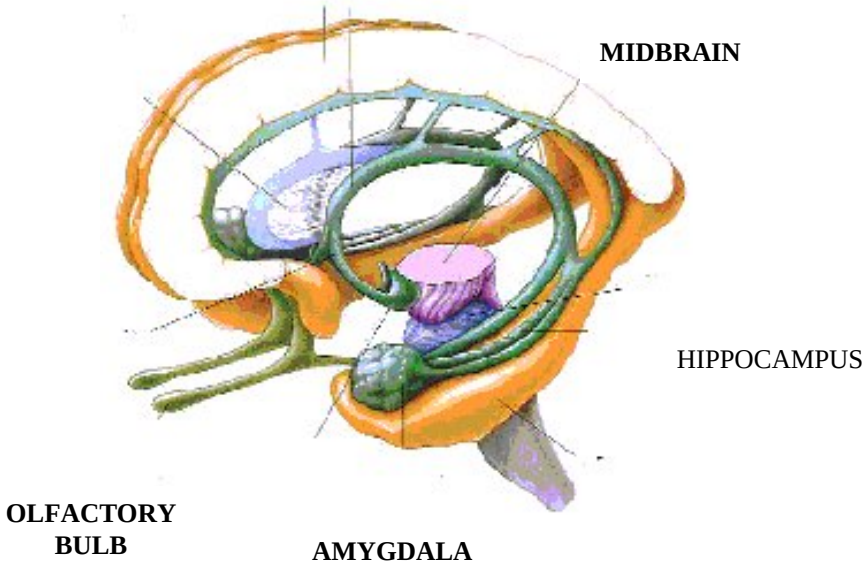
FACIAL EXPRESSION
EYE MOVEMENT
BALANCE

HEART RATE
RESPIRATION
BLOOD PRESSURE
TEMPERATURE
SWALLOWING
VOMITING



THE LIMBIC SYSTEM





THE MAJOR SYSTEM AFFECTED BY CHEMICAL EXPOSURES MCS.

VOLATILE CHEMICALS ACCESS THE BRAIN DIRECTLY VIA THE OLFACTORY BULB MND? J8

AN APPLE A DAY = AN EFFECTIVE DOSE OF A HERBICIDE/PESTICIDE

USING A RADIOLABELLED DFP TRACER AND RADIOLABELLED PESTICIDE MOLECULES AND ACCELERATED MASS SPECTROMETRY

INCREASED MOVEMENT OF TRACER MOLECULE INTO BRAIN TISSUE FOLLOWING VERY LOW EXPOSURE TO PESTICIDE

BRAIN (pg/g tissue) detection limits attomolar 10^{-18}

DFP	+PTN	+PER	+BOTH
4.09	5.42	5.19	5.85

RBCs, PLASMA, MUSCLE, LIVER , SPLEEN ALSO

"These data show that common pesticides significantly change the amount of toxin at concentrations provided by oral exposure doses commensurate with the normal ingestion of sprayed foods, drinking of surface water, or use of home pesticides that would not be measurable in traditional assays"

"Mechanism involves greater BBB permeability leading to neural damage- other toxins and even pathogens may also obtain greater access."

Vogel et al Env Health Perspect 2002;110 suppl:1-5

OTHER REPORTS

NON-HODGKINSON'S LYMPHOMA - SWEDEN

ANTI-CHOLINESTERASE ACTIVITY

IRRITATION OF EYES AND CORNEA

DISRUPTION OF KEY FUNCTIONAL ENZYMES (NADPH) IN PREGNANT RATS AND THEIR FOETUSES

GLYPHOSATE MODERATELY TOXIC TO FISH BUT FORMULATED PRODUCT ~3 x MORE

SOIL ORGANISMS- 59% OF SCREENED ORGANISMS INHIBITED

MYCORRHIZAE INHIBITED ALLOWING OVERGROWTH OF TOXIC FUSARIUM SPP. RESULTING IN CROP LOSS

DESTROYS N-FIXING BACTERIA

NOT IRREVERSIBLY BOUND TO SOIL - RECIRCULATES

PERSISTENCE IN SOIL AND WATER HIGH

1-174; 55-360 DAYS; 10-12 WEEKS T 1/2 POND WATER

POND RESIDUE 400 DAYS

ACCEPTABLE DAILY INTAKE- ADI = 0.01 mg/kg (1985)

BASED ON NOEL [No Observable Effect Level] IN RATS WITH A 100-FOLD SAFETY MARGIN.

EQUATES TO MPI [Maximum Permitted Intake] 6 mg/kg FOR A 60 kg MAN

TMRC [Theoretical Maximum Residue Contribution] CALCULATED AS 1.39 mg/day FOR A 1.5 kg DAILY DIET

TOLERANCES FOR RESIDUES ppm

	1982	1997	2001
Barley	**0.1**	**20**	**20**
Wheat	**0.1**	**5**	**5**
Soyabean Hay	**15**	**200**	**200**

EPA - 1982 "Maximum residue tolerances in most foods for DIRECT CONSUMPTION whether meat, fruit or vegetable, are around 0.2 ppm……although in grain products…lower 0.1 ppm" -WHY?

FEEDING STUDIES SHOW THAT GLYPHOSATE ACCUMULATES IN BONE > 10x OTHER ORGANS

BONE PROVIDES A SINK FOR GLYPHOSATE-CUMULATIVE TOXICITY → OSTEOPOROSIS?

ADD ONS -

MARKER GENES

ANTIBIOTICS- PENICILLINS, AMINOGLYCOSIDES

β–GLUCURONIDASE

BIG QUESTIONS

ROUTES ADMINISTRATION

CUMULATIVE TOXICITY

SYNERGISM - ABOU-DONIA, HOWARD

KEY SYSTEMS NOT INVESTIGATED -GUT etc

SOURCES OF INFORMATION

http://www.rag.au/modifiedfoods/roundup

http://www.naturecountrystore.com/roundup/

http://www.abcbirds.org/pesticides/Profiles/glyphosate.htm

http://www.ucsuas.org/food_and_environment/biotechnology/

ALL THESE PROVIDE A NUMBER OF REFERENCES INCLUDING THOSE COVERING THE ISSUES I HAVE PRESENTED IN THIS TALK.

A LIST OF OTHER REFERENCES IS ATTACHED