Parkinson’s disease (“Shaking Palsy”), described by English doctor James Parkinson in 1817, is a neurodegenerative disease caused by death of dopaminergic neurons and astrocytes in the substantia nigra of the brain, with increase in the number of microglia immune cells there (inflammatory reaction). The substantia nigra (SN) is one of five basal ganglia structures in the midbrain behind the pituitary, and plays an important role in reward and movement. (Substantia nigra cells appear darker due to high levels of neuromelanin there.)

In the presymptomatic stage of Parkinson’s, years before diagnosis, “Lewy bodies” (abnormal aggregation of alpha-synuclein protein) first appear in the olfactory bulb cells (with decreased sense of smell). Then these changes appear in the medulla and pons (Braak staging: Mov Disord. 2006 Dec;21(12):2042-51) with early non-motor symptoms (poor sleep, fatigue, depressed mood, and autonomic dysfunction). As the disease progresses, Lewy bodies also develop in the substantia nigra, causing motor dysfunction when up to 50–80% of the substantia nigra’s dopaminergic neurons have died, with resting tremor, muscle rigidity, slow movement, and postural instability. Then it can continue to the neocortex, causing thinking and behavioral problems and Lewy body dementia. (This is distinguished from Alzheimer’s disease where neurons accumulate tau protein aggregations).

Dopaminergic neuron cell death in Parkinson’s is associated with molecular damage in their mitochondrial complex 1 (ATP energy production), with intracellular Lewy bodies (aggregations of alpha-synuclein protein), and also with decreased calcium ion transport out of the cell. Neuron firing is triggered by calcium ion influx through calcium channels, but excess calcium accumulation in cells (from toxic cell-membrane damage, ATP deficiency, and/or over-excitation of the neurons) causes buildup of oxidative stress damage to the cell molecules, triggering apoptosis (cell death).

The olfactory bulb sensory input comes from olfactory receptor neurons in the olfactory epithelium (upper nasal cavity bilaterally), and acts as a filter sending signals to higher brain processing centers, as well as receiving input from the substantia nigra. Not surprisingly, risk of Parkinson’s disease is increased with exposure to Volatile Organic Compounds (VOCs) such as aerosol pesticides that enter through the nose, as well as from prior head injuries (boxer Mohamed Ali).

The cribriform plate in the ethmoid bone at the apex of the nasal cavity, through which the olfactory neurons pass, is the only part of the brain without a protective blood-brain barrier. Toxic molecules in the nasal cavity can pass along these nerves there directly into the cerebrospinal fluid (see diagrams below), and then 1 or 2 cm posteriorly along the olfactory tract to the optic chiasm (where the optic nerves cross) and the pituitary gland (which controls the body’s hormone function). Behind the pituitary is the cerebral peduncle containing the substantia nigra that regulates motor function.

This fluid pathway duplicates the chronological order of the development of Parkinson’s pathology, and explains its relationship to inhaled toxic VOC molecules, with the damage slowly developing over years before the diagnosis. Susceptibility depends on not only the severity and duration of exposure, but also on nutritional status and inherited genetic deficiencies in detoxification enzymes. Chronic Inflammatory Response Syndrome (Dr Ritchie Shoemaker) also begins on this pathway. Healthful lifestyles (good nutrition and avoiding toxic exposure) are the best prevention.

Dr Bradford, 201904
**Nasal cavity**, showing olfactory nerves (sense of smell) penetrating the nasal cavity roof and into the cerebrospinal fluid that surrounds the brain. Inflammatory molecules can easily follow this fluid pathway posteriorly to the pituitary gland and hypothalamus, and to the optic chiasm (where the optic nerves cross). Inflammation in these centers causes impaired pituitary hormone function, immune problems, and decreased Visual Contrast Sensitivity (the online VCS test).
Brain inferior view:
Inflammatory molecules in the cerebrospinal fluid bathing this area easily move further posteriorly to the cerebral peduncle containing the substantia nigra (the brain center for muscle tone regulation). Cells in this area are chemically damaged in Parkinson’s disease, which is highly correlated with past exposure to pesticide fumes. In the Parkinson’s form of dementia (Lewy Body Dementia), this damage spreads further to cells in the neocortex area.