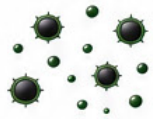
NEUROGENIC INFLAMMATION CASCADE

How Environmental Irritants Drive Nervous System-Mediated Inflammation

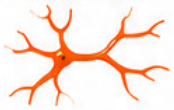
In susceptible or sensitized individuals, environmental irritants can activate sensory nerves—triggering neuropeptide release, amplifying inflammation, and contributing to multi-system effects.

1 IRRITANTS



VOCs, MVOCs, particles, fumes, combustion byproducts, aerosols, mold fragments, etc.

2 SENSORY NERVE ACTIVATION



Trigeminal nerve & peripheral afferents (C-fibers, Aδ fibers)

3 NEUROPEPTIDE RELEASE

Substance P, CGRP, Neurokinin A and others

4 VASCULAR & IMMUNE EFFECTS

Vasodilation, increased permeability, immune cell activation

5 SYMPTOMS (MULTI-SYSTEM)

Symptoms across multiple systems

1 ENVIRONMENTAL TRIGGERS

Common exposures include:

- VOCs and MVOCs
- Mold particles and fragments
- Smoke, combustion byproducts, fumes
- Dust and airborne particulates
- Cleaning agents and fragranced products

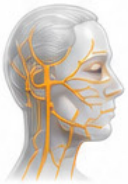
PRIMARY ENTRY POINTS

- Inhalation (airway epithelium)
- Ocular surface
- Skin contact

2 SENSORY NERVE ACTIVATION

(Trigeminal & Peripheral Afferents)

Environmental irritants stimulate nociceptive sensory nerves, particularly the trigeminal nerve (CN V), which detects chemical and particulate irritants in the nose, sinuses, eyes, and face.



Primary pathways:

- Trigeminal nerve (cranial nerve V)
- C-fibers (unmyelinated)
- Aδ fibers (thinly myelinated)

Key mechanism:
Irritants activate ion channels such as TRPA1 and TRPV1, responsible for chemical irritation (chemosthesis). Activation can occur rapidly (seconds to minutes). Signals are transmitted locally and to the central nervous system.

3 NEUROPEPTIDE RELEASE

Activated sensory nerves release signaling molecules into surrounding tissue.

Key neuropeptides:

- Substance P (SP)
- CGRP
- Neurokinin A (NKA)
- Others

These molecules act as local amplifiers, linking the nervous system to vascular and immune responses.

4 LOCAL VASCULAR & IMMUNE EFFECTS

Neuropeptides drive measurable physiological responses:

Vasodilation
Increased blood flow, redness

Increased vascular permeability
Fluid leakage, swelling

Mast cell activation
Release of histamine and inflammatory mediators

Immune cell recruitment
Neutrophils, eosinophils, and other immune cells

5 SYMPTOMS (MULTI-SYSTEM)

Neurogenic inflammation may contribute to symptoms across multiple systems:

Central nervous system
Brain fog, headaches, sensory sensitivity

Autonomic system
HR/BP variability, dysregulation

Respiratory system
Irritation, congestion

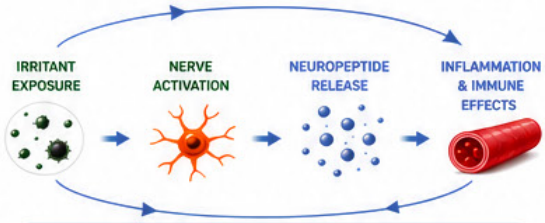
Gastrointestinal system
Motility changes, sensitivity

Musculoskeletal system
Tension, discomfort

Skin / mast cell activity
Flushing, itching, reactivity

6 SELF-AMPLIFYING FEEDBACK LOOP (SENSITIZATION)

Inflammation and neuropeptide signaling further activate sensory nerves, lowering the threshold for future responses.



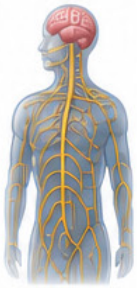
RESULT: Heightened reactivity and symptom persistence, even at lower exposure levels.

7 SYSTEMIC SIGNALING & NERVOUS SYSTEM EFFECTS

Neurogenic inflammation is not confined to the initial site of exposure. Through neural and inflammatory signaling, it may influence multiple systems.

MECHANISMS

- Trigeminal nerve signaling (facial & airway sensory pathways)
- Peripheral-to-central neural signaling
- Central sensitization (including microglial activation in the brain and spinal cord)
- Autonomic nervous system involvement



POTENTIAL EFFECTS ACROSS SYSTEMS

- Central nervous system: Brain fog, headaches, sensory sensitivity
- Autonomic system: HR/BP variability, dysregulation
- Respiratory system: Irritation, congestion
- Gastrointestinal system: Motility changes, sensitivity
- Musculoskeletal system: Tension, discomfort
- Skin / mast cell activity: Flushing, itching, reactivity

8 SENSITIZATION PROCESS (PROGRESSION OVER TIME)

Not all individuals respond this way. Sensitization develops over time in some people.

9 WHO IS MOST AFFECTED?

This pattern is more likely in individuals with:

- Prior significant exposure (e.g., water-damaged environments, chemical exposure)
- Repeated or chronic low-level exposures
- Existing inflammatory or allergic conditions
- Nervous system sensitization (lower response threshold)

Individual factors such as genetics, age, stress, and coexisting conditions may influence risk and severity.

10 KEY TAKEAWAY

Environmental irritants do not only affect tissues—they can activate the nervous system. Through neuropeptide signaling and immune–vascular interactions, this may drive a self-amplifying cascade contributing to inflammation and multi-system symptoms—particularly in sensitized individuals.

REFERENCES:

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