POST-VIRAL GASTROINTESTINAL DISRUPTION & DYSFUNCTION

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Disclosures
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Disclosures
There are currently no FDA approved therapeutics in this clinical space.
These recommendations are based on clinical expertise of post-infectious disorders.
KEY CONCEPTS

The nervous, immune, & endocrine systems play integral roles in maintaining physiological homeostasis.

Within tissues* neurons, immune & endocrine cells are in close physical proximity.

• *Consider the implications of connective tissue disorders

There is bidirectional communication between neurons, immune & endocrine cells.
POST-VIRAL GASTROINTESTINAL SYMPTOMS

- Nausea, headache, cognitive changes, rhinorrhea, oral tingling | burning, dry mouth
- Dysphagia, belching, abdominal pain, abdominal bloating, early satiety, constipation, straining with defecation, diarrhea
- Adverse reactions to food, flushing, urticaria, rash

These symptoms are driven by disturbances in the neuroimmune axis.
Defining the neuroimmune axis
NEUROANATOMY OF THE GASTROINTESTINAL TRACT

AUTONOMIC NERVOUS SYSTEM

ENTERIC NERVOUS SYSTEM
NEUROANATOMY OF THE ENTERIC NERVOUS SYSTEM

THE ENTERIC NERVOUS SYSTEM IS A PART OF THE AUTONOMIC NERVOUS SYSTEM

DOI: 10.1038\NRGASTRO.2012.32
FUNCTIONS OF THE GASTROINTESTINAL TRACT

- Food bolus processing
- Macromolecule breakdown
- Nutrient absorption
- Water absorption
- Waste storage
- Water absorption
- Stool formation

FUNCTIONS OF THE GASTROINTESTINAL TRACT

Mucosal barrier regulation
Immune training
Neuroimmune axis communication

THE GASTROINTESTINAL TRACT – LARGEST INTERFACE OF THE NERVOUS, IMMUNE, & ENDOCRINE SYSTEMS
THE CRITICAL GASTROINTESTINAL INTERFACE
The neuroimmune axis in action

A few examples.
NEUROIMMUNE CROSSTALK – REGULATING GASTROINTESTINAL MOTILITY AND CELL SURVIVAL

CSF1 – COLONY STIMULATING FACTOR 1
BMP2 – BONE MORPHOGENIC PROTEIN 2
NEUROIMMUNE CROSSTALK – CRITICAL FOR ENTERIC NEURON SURVIVAL DURING INFECTION

Extrinsic sympathetic neurons → B2AR → Polyamines → Enteric neurons

NOREPINEPHRINE

B2AR – B2 ADRENERGIC RECEPTOR

DOI: 10.1038/s41385-020-00368-1
NEUROIMMUNE CROSSTALK – CRITICAL FOR ENTERIC NEURON SURVIVAL DURING INFECTION
NEUROIMMUNE CROSSTALK – MAST CELL DEGRANULATION IS NOT JUST AN IgE MEDIATED PROCESS
Our gut microbiota is communicating with our nervous, immune, & enteroendocrine systems.
Substances secreted by microbes enter the bloodstream and travel to the CNS.

Microbes activate enteroendocrine cells (neuropods) which synapse with the ENS and ANS which in turn communicate with the CNS.

Microbes activate enteroendocrine cells which then release hormones that have local and distant effects.

Microbes influence immune cell function and inflammation affecting the functions of the ENS, ANS, and CNS.
Neuroimmune axis disorders – A systems biology way of thinking about complex conditions.

Will help us accelerate research and clinical care.

Requires next generation tools for diagnosis.
Making the diagnosis requires leading edge diagnostic tools.

Specialist referral is required.
NEXT GENERATION - MOTILITY TESTING

SmartPill wireless motility capsule

DIAGNOSE REGIONAL & WHOLE GUT MOTILITY DISORDERS
NEXT GENERATION BIOPSY TECHNIQUES – FULL THICKNESS BIOPSIES

SAMPLES THE ENTIRE THICKNESS OF THE GASTROINTESTINAL TRACT WALL

DOI: 10.4253/wjge.v12.i6.193
TISSUE LEVEL ENTERIC NERVOUS SYSTEM MAPPING | EVALUATION

DIAGNOSE GASTROINTESTINAL NEUROPATHIES
DIAGNOSE DEEP TISSUE LEVEL IMMUNE DISORDERS

DOI: 10.1053/j.gastro.2020.02.035.
TISSUE LEVEL IMMUNE PROFILING

PROVIDES VALUABLE INFORMATION FOR SELECTION OF THERAPEUTIC AGENTS
DIAGNOSING NEUROIMMUNE DISORDERS


Mast cells
Emerging diagnostic tools – Diagnosing non-IgE mediated allergies.
People suffering from digestive signs, I know abnormal area.

Signs moving ordered.

Symptoms mainly (defecating content accommodate relieved frequency).
"IRRITABLE BOWEL SYNDROME"

- Impacts 15-20% of the global population.
- 50% contemplate suicide. This is not a benign condition.
- Functional gastrointestinal disorders are disorders of the neuroimmune axis.
DIAGNOSING NON-IGE MEDIATED ALLERGIES

BEFORE ALLERGEN EXPOSURE

AFTER ALLERGEN EXPOSURE

CLE – CONFOCAL LASER ENDOMICROSCOPY

DOI: 10.1053/j.gastro.2019.03.046.
DOI: 10.1053/j.gastro.2014.07.046.
Many Patients With Irritable Bowel Syndrome Have Atypical Food Allergies Not Associated With Immunoglobulin E

Annette Fritscher-Ravens,¹ Theresa Pflaum,¹ Marie Mösinger,¹ Zino Ruchay,¹ Christoph Röcken,² Peter J. Milla,³ Melda Das,¹ Martina Böttner,⁴ Thilo Wedel,⁴ and Detlef Schuppan⁵,⁶

70% tested positive for a non-IgE mediated allergy

- Allows for detection of specific antigen
- Allows for a truly prescriptive diet

Detects alterations in mucosal barrier

- Currently missed by routine histology (H&E)

Detects eosinophil activation

- May also detect mast cell activation
- Mast cells are likely involved in both IgE and non-IgE mediated allergies

50% of patients with IBS may have a non-IgE mediated allergy
Improving the diagnosis through discovering the mechanism of dysfunction.

Expands therapeutic options.

Moves beyond symptomatic management.
IN SUMMARY

- Gastrointestinal symptoms are common in Post-viral disorders; disorders of the neuroimmune axis.
- Specialist referral is required.
- We need to leverage leading technologies to improve diagnostics and therapeutics for these disorders.
- Early recognition, thorough diagnosis, and targeted interventions are essential to improve patient outcomes.
REFERENCES


