Base Hits

with Dr. Tom O'Bryan



# Changing the Direction of Your Nervous System from Fight, Flight or Fright to Calm, Regenerative Healing

## Session 2:
## Thyroid: Take the Deep Dive on Thyroid Health

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- ***Scientific Advisory Board - International and American Association of Clinical Nutritionists***

**It is not the stress itself, but how the body reacts or responds to that stress that is the problem.**

# Premise #1

**In order to make it 'easy to do the right thing', we must understand how and why we've gotten to where we are, if we want to stop the development of disease**



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## Professor Alessio Fasano

- Professor of Pediatrics at Harvard Medical School
- Professor of Nutrition at Harvard T.H. Chan School of Public Health
- Chief of Pediatric Gastroenterology, Mass General Hospital
- Director, Mucosal Immunology Center, Harvard
- Director, Center for Celiac Research and Treatment
- Director, Mucosal Immunology and Biology Research Center;
- Associate Chief for Basic, Clinical and Translational Research
- 213 publications on pubmed.gov
- Identified zonulin as the protein activated in intestinal permeability





F1000Research 2020, 9(F1000 Faculty Rev):69 Last updated: 31 JAN 2020

REVIEW

**All disease begins in the (leaky) gut: role of zonulin-mediated gut permeability in the pathogenesis of some chronic inflammatory diseases [version 1; peer review: 3 approved]**

Alessio Fasano [1,2]

[1]Mucosal Immunology and Biology Research Center, Center for Celiac Research and Treatment and Division of Pediatric Gastroenterology and Nutrition, Massachusetts General Hospital for Children, Boston, Massachusetts, USA
[2]European Biomedical Research Institute of Salerno, Salerno, Italy

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**Abstract**

Improved hygiene leading to reduced exposure to microorganisms has been implicated as one possible cause for the recent "epidemic" of chronic inflammatory diseases (CIDs) in industrialized countries. That is the essence of the hygiene hypothesis that argues that rising incidence of CIDs may be, at least in part, the result of lifestyle and environmental changes that have made us too "clean" for our own good, so causing changes in our microbiota. Apart from genetic makeup and exposure to environmental triggers, inappropriate increase in intestinal permeability (which may be influenced by the composition of the gut microbiota), a "hyper-belligerent" immune system responsible for the tolerance–immune response balance, and the composition of gut microbiome and its epigenetic influence on the host genomic expression have been identified as three additional elements in causing CIDs. During the past decade, a growing number of publications have focused on human genetics, the gut microbiome, and proteomics, suggesting that loss of mucosal barrier function, particularly in the gastrointestinal tract, may substantially affect antigen trafficking, ultimately influencing the close bidirectional interaction between gut microbiome and our immune system. This cross-talk is highly influential in shaping the host gut immune system function and ultimately shifting genetic predisposition to clinical outcome. This observation led to a re-visitation of the possible causes of CIDs epidemics, suggesting a key pathogenic role of gut permeability. Pre-clinical and clinical studies have shown that the zonulin family, a group of proteins modulating gut permeability, is implicated in a variety of CIDs, including autoimmune, infective, metabolic, and tumoral diseases. These data offer novel therapeutic targets for a variety of CIDs in which the zonulin pathway is implicated in their pathogenesis.

**Keywords**

Chronic inflammatory diseases, Gut permeability, microbiome, zonulin

Open Peer Review

Reviewer Status

| | Invited Reviewers | | |
|---|---|---|---|
| | 1 | 2 | 3 |
| version 1 | | | |

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2 **Michael Mees**, Chulalongkorn University, Bangkok, Thailand
3 **Arul Jayaraman**, Texas A&M Health Science Center, Bryan, USA

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5

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Alessio Fasano [1,2]

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[2]European Biomedical Research Institute of Salerno, Salerno, Italy

**There is growing evidence that the elements of gut permeability, immune system response, and gut microbiome—together with genetic predisposition and exposure to environmental triggers— make the *"perfect storm"* for Chronic Inflammatory Disease development.**

in causing CIDs. During the past decade, a growing number of publications have focused on human genetics, the gut microbiome, and proteomics, suggesting that loss of mucosal barrier function, particularly in the gastrointestinal tract, may substantially affect antigen trafficking, ultimately influencing the close bidirectional interaction between gut microbiome and our immune system. This cross-talk is highly influential in shaping the host gut immune system function and ultimately shifting genetic predisposition to clinical outcome. This observation led to a re-visitation of the possible causes of CIDs epidemics, suggesting a key pathogenic role of gut permeability. Pre-clinical and clinical studies have shown that the zonulin family, a group of proteins modulating gut permeability, is implicated in a variety of CIDs, including autoimmune, infective, metabolic, and tumoral diseases. These data offer novel therapeutic targets for a variety of CIDs in which the zonulin pathway is implicated in their pathogenesis.

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the *"perfect storm"*
for Chronic Inflammatory Disease development.



## the *"perfect storm"* for Chronic Inflammatory Disease development.

- Genetic Vulnerability
- Environmental triggers
- Altered Microbiome (Dysbiosis)
- Intestinal Permeability
- Systemic Immune Response (Innate and Adaptive)

# If there is 1 concept, that becomes the foundational paradigm you look through, for all chronic inflammatory diseases, this is it





## the *"perfect storm"* for Chronic Inflammatory Disease development.

- Genetic Vulnerability
- Environmental triggers
- Altered Microbiome (Dysbiosis)
- Intestinal Permeability
- Systemic Immune Response (Innate and Adaptive)

# Although there are likely dozens of environmental triggers that have contributed to your specific inflammatory state, what's the 'Big Kahuna'?



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**Open Peer Review**

**Reviewer Status** ✓ ✓ ✓

**Among the several potential intestinal luminal stimuli that can stimulate zonulin release (thus Intestinal Permeability), small exposure to large amounts of bacteria (and its exhaust LPS) and gluten, have been identified as the two most powerful triggers**

gastrointestinal tract, may substantially affect antigen trafficking, ultimately influencing the close bidirectional interaction between gut microbiome and our immune system. This cross-talk is highly influential in shaping the host gut immune system function and ultimately shifting genetic predisposition to clinical outcome. This observation led to a re-visitation of the possible causes of CIDs epidemics, suggesting a key pathogenic role of gut permeability. Pre-clinical and clinical studies have shown that the zonulin family, a group of proteins modulating gut permeability, is implicated in a variety of CIDs, including autoimmune, infective, metabolic, and tumoral diseases. These data offer novel therapeutic targets for a variety of CIDs in which the zonulin pathway is implicated in their pathogenesis.

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Clinical Review & Education

JAMA | Review

# Celiac Disease and Nonceliac Gluten Sensitivity
## A Review

Maureen M. Leonard, MD, MMSc; Anna Sapone, MD, PhD; Carlo Catassi, MD, MPH; Alessio Fasano, MD

**IMPORTANCE** The prevalence of gluten-related disorders is rising, and increasing numbers of individuals are empirically trying a gluten-free diet for a variety of signs and symptoms. This review aims to present current evidence regarding screening, diagnosis, and treatment for celiac disease and nonceliac gluten sensitivity.

**OBSERVATIONS** Celiac disease is a gluten-induced immune-mediated enteropathy characterized by a specific genetic genotype (*HLA-DQ2* and *HLA-DQ8* genes) and autoantibodies (antitissue transglutaminase and antiendomysial). Although the inflammatory process specifically targets the intestinal mucosa, patients may present with gastrointestinal signs or symptoms, extraintestinal signs or symptoms, or both, suggesting that celiac disease is a systemic disease. Nonceliac gluten sensitivity is diagnosed in individuals who do not have celiac disease or wheat allergy but who have intestinal symptoms, extraintestinal symptoms, or both, related to ingestion of gluten-containing grains, with symptomatic improvement on their withdrawal. The

and the development of possible comorbidities.

*JAMA*. 2017;318(7):647-656. doi:10.1001/jama.2017.9730

CME Quiz at jamanetwork.com/learning

**Author Affiliations:** Center for Celiac Research and Treatment, Division of Pediatric Gastroenterology and Nutrition, MassGeneral Hospital for Children, Boston, Massachusetts (Leonard, Sapone, Catassi, Fasano);

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**Section Editors:** Edward Livingston, MD, Deputy Editor, and Mary McGrae McDermott, MD, Senior Editor.

**Previous studies have shown that gliadin (in wheat) can cause an immediate and transient increase in gut permeability. This process takes place <u>in all individuals</u> who ingest gluten.**

Celiac disease is a chronic, small-intestinal immune-mediated enteropathy initiated by exposure to dietary gluten in genetically predisposed individuals and characterized by specific autoantibodies against tissue transglutaminase 2 (anti-tTG2), endomysium, and/or deamidated gliadin peptide.[1] Although up to 40% of the population carries the genotype *HLA-DQ2* or *HLA-DQ8*, which is required for the development of celiac disease, only 2% to 3% of *HLA-DQ2* or *HLA-DQ8* carriers subsequently develop celiac disease.[2] Celiac disease, once considered a relatively rare gastrointestinal condition affecting almost exclusively young white children, can develop at any age and can affect almost any race. Celiac disease was first described by Samuel Gee in 1887. Wheat was hypothesized as the possible offending agent by William Dicke in 1941.[3]

The epidemiology, clinical presentation, pathophysiology, and management of the disease have changed since its initial description. There is strong evidence that celiac disease is an autoimmune disease triggered by the ingestion of gluten present in wheat, barley, and rye in genetically predisposed individuals. The prevalence of celiac disease in the general population is 1%, with regional differences (**Table 1**).[4] Celiac disease can affect any human organ or tissue (Table 1 and **Table 2**).[6]

*Nonceliac gluten sensitivity* is a term used to describe individuals who have intestinal signs or symptoms, extraintestinal signs or symptoms, or both, related to ingestion of gluten-containing grains (Table 2), with improvement when these are removed from a patient's diet. The frequency of nonceliac gluten sensitivity is unknown owing to the lack of validated biomarkers, but it is thought to be more common than celiac disease. Wheat allergy, the third gluten-related disorder, which will not be addressed in this review, is defined as an adverse type-2 helper T-cell immunologic reaction to wheat proteins and typically presents soon after wheat



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ORIGINAL PAPERS

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Iva Brynychova[1, B–D, F], Iva Hoffmanova[2, E, F], Milos Dvorak[3, E, F], Pavlina Dankova[1, A, C, E, F]

# Increased Expression of TLR4 and TLR7 but Not Prolactin mRNA by Peripheral Blood Monocytes in Active Celiac Disease*

[1] Department of Anthropology and Human Genetics, Faculty of Science, Charles University in Prague, Czech Republic
[2] Second Department of Internal Medicine, Third Faculty of Medicine, Charles University in Prague, Czech Republic
[3] First Medical Faculty, Charles University in Prague and General University Hospital in Prague, Czech Republic

**A** – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation;

**Gliadin fragments have been identified to activate the innate immune system *via* TLR4**

clinical signs and symptoms of CD improve after the introduction of a gluten-free diet (GFD). The focus was on changes in mRNA expression of selected toll-like receptors (TLR2, TLR4, TLR7), stress cytokine prolactin (PRL), and pro- and anti-inflammatory cytokines (TNF-α, IL-6, IL-12, IL-10) in PBMs.

**Material and Methods.** The study involved 20 CD patients diagnosed according to the European Society for Pediatric Gastroenterology, Hepatology and Nutrition criteria and Marsh criteria: 10 recently-diagnosed cases (rCD) and 10 on a GFD for a minimum of one year. The control group comprised 10 age- and sex-matched healthy volunteers. PBMs from peripheral blood specimens were separated using immunomagnetic CD14+ beads. Total RNA was isolated using a standard commercial kit. Cytokine and TLR mRNA levels were quantified by relative qPCR with *PGK1* as a reference gene.

**Results.** Significantly higher expression of TLR4 and TLR7 mRNA was observed in PBMs from rCD patients compared to the healthy controls (1.63 times higher; $p < 0.05$). TLR7 mRNA levels in rCDs were also significantly elevated in comparison to the CD-GFD patients (2.11 times higher; $p < 0.01$). TNF-α mRNA expression tended to be higher in both groups of patients; by contrast, in IL-6 mRNA, a trend to a fourfold decrease was detected in PBMs from the CD-GFD subjects. IL-10, IL-12 and PRL levels did not differ among the groups.

**Conclusions.** The data suggest that the inflammatory process in rCD intestinal mucosa and submucosa reflecting enterocyte damage can be detected in PBMs in peripheral blood. Further, the cytokine and TLR expression profile in PBMs alters after one year of GFD treatment (**Adv Clin Exp Med 2016, 25, 5, 887–893**).

**Key words:** celiac disease, monocytes, cytokines, prolactin, innate immunity.

Celiac disease (CD) is defined as the loss of oral tolerance to gluten in genetically predisposed individuals; it is an organ-specific autoimmune disease with a prevalence of about 1% in Europe [1]. Clinical manifestation of the gluten-induced inflammatory response in celiac mucosa is highly variable and can occur both in childhood and in adulthood. The only possible treatment of CD is a lifelong gluten-free diet (GFD).

Imbalance in the innate immune mechanisms is known to contribute to the pathogenesis of CD.

* This study was funded by the Grant Agency of Charles University in Prague (grant 316211).

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## Abstract

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3 **Arul Jayaraman**, Texas A&M Health Science Center, Bryan, USA

Any comments on the article can be found at the end of the article.

**Gluten is misinterpreted by the zonulin pathway as a potential harmful component of a microorganism.**





https://f1000research.com/articles/9-69/v1



*Physiol. Res. 52: 79-88, 2003*

# IgA and IgG Antigliadin, IgA Anti-tissue Transglutaminase and Antiendomysial Antibodies in Patients with Autoimmune Thyroid Diseases and Their Relationship to Thyroidal Replacement Therapy

J. JISKRA, Z. LÍMANOVÁ, Z. VANÍČKOVÁ[1], P. KOCNA[1]

*Third Medical Department and [1]Department of Clinical Biochemistry, First Medical Faculty*

**With AI Thyroid Disease, IgA antigliadin ABs in 15.98 %, IgG antigliadin antibodies in 51.48 %, and IgA anti-tissue transglutaminase in 14.79 %.**

**Summary**

Celiac disease is a chronic illness of the small bowel caused by gliadin intolerance in genetically predisposed subjects. The aim of this study was to investigate serum levels of IgA and IgG antigliadin antibodies, IgA antiendomysial antibodies, and IgA anti-tissue transglutaminase antibodies in 169 patients with autoimmune thyroid diseases, i.e. chronic thyroiditis and Graves´ disease. Antiendomysial antibodies were positive in 2 out of 169 persons (1.18 %), IgA antigliadin antibodies in 15.98 %, IgG antigliadin antibodies in 51.48 %, and IgA anti-tissue transglutaminase in 14.79 %. The prevalence of positivity was higher compared to the 1312 control blood donors described in our previous study (Vančíková *et al*. 2002) ($p<0.05$). Patients with chronic thyroiditis treated with a high replacement dosage of levothyroxin (125-200 µg daily) had higher serum levels of IgA antigliadin antibodies in comparison with patients treated with a lower dosage (50-100 µg daily) (medians: 13.00 vs. 19.69, $p=0.033$). We found a negative correlation of IgA anti-tissue transglutaminase antibodies and total calcium serum levels ($r = –0.480$, $p=0.0236$, $n=22$). We can conclude that in persons with autoimmune thyropathy there is a high prevalence of positive antigliadin, anti-tissue transglutaminase and antiendomysial antibodies. Latent celiac disease may lead to impaired resorption of therapeutically administered levothyroxine, calcium, or other substances.

J Clin Endocrin Metab. First published ahead of print January 11, 2012 as doi:10.1210/jc.2011-1851



# Atypical Celiac Disease as Cause of Increased Need for Thyroxine: A Systematic Study

Camilla Virili, Giulia Bassotti, Maria Giulia Santaguida, Raffaella Iuorio, Susanna Carlotta Del Duca, Valeria Mercuri, Antonio Picarelli, Patrizia Gargiulo, Lucilla Gargano, and Marco Centanni

Endocrinology Section, Department of Medico-Surgical Sciences and Biotechnologies (C.V., M.G.S., S.C.D.D., M.C.), Department of Experimental Medicine (G.B., R.I., V.M., P.G.), and Gastroenterology Unit, Department of Internal Medicine and Medical Specialties (A.P.), "Sapienza" University of Rome, 00161 Rome, Italy; and Endocrinology Unit (L.G., M.C.), Azienda Unità Sanitaria Locale di Latina, 04100 Latina, Italy

**Objective:** Replacement $T_4$ dose in hypothyroid patients bearing both chronic autoimmune thyroiditis and atypical celiac disease (CD) has been analyzed.

in all patients after 5 ± 2 months of treatment at a median $T_4$ dose of 1.31 $\mu$g/kg·d. After a similar period and dose of $T_4$, higher levels of TSH (median = 4.20 mU/liter) were observed in patients with HT and CD. In 21 CD patients, target TSH (median TSH = 1.25 mU/liter) has been attained after 11 ± 3 months of GFD without increasing $T_4$ dose (1.32 $\mu$g/kg·d). In the remaining 14 patients, who were noncompliant with GFD, target TSH has also been achieved but at a higher $T_4$ dose (median = 1.96 $\mu$g/kg · d; +49%; $P$ = 0.0002) than in hypothyroid patients without CD.

**Conclusions:** Atypical CD increases the need for $T_4$. The effect was reversed by GFD or by increasing $T_4$ dose. Malabsorption of $T_4$ may provide the opportunity to detect CD that was overlooked until the patients were put under $T_4$ therapy. (*J Clin Endocrinol Metab* 97: E0000–E0000, 2012)

**In patients with HT and CD not compliant with GFD, the therapeutic dose of T4 should be increased by almost 50%.**

The therapeutic target of oral $T_4$ treatment is to achieve the expected serum TSH concentration as a marker of thyroid homeostasis. Failure to reach this goal represents a diagnostic puzzle because several conditions may interfere with this hormonal treatment (for review, see Refs. 1–3 and http://www.hotthyroidology.com/editorial_169.html). Oral $T_4$ absorption is key to pharmacological thyroid homeostasis (4, 5). The increased daily requirement of $T_4$ dose has been recently correlated with the presence of gastric diseases (3, 6). However, an increased need for $T_4$ may even occur in intestinal disorders (7), namely celiac disease (CD), a permanent gluten intolerance of the small intestinal mucosa, whose histopathological grading has been repeatedly classified (7, 8). The spectrum of clinical features also extends from asymptomatic forms to overt disease (9–11), classified into five phenotypes (7, 12). The "atypical" phenotype can account for more than half of all cases and, due to little or no gastrointestinal symptoms, may remain occult for years (12, 13). Hence, overt CD is the tip of an iceberg because only 10–20% of cases of histologically diagnosed CD are identified on the basis of clinical findings (9), and its true prevalence ap-

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Abbreviations: CD, Celiac disease; GFD, gluten-free diet; HT, Hashimoto's thyroiditis; IQ1–IQ3, Interquartile range; TPOAb, thyroid peroxidase antibodies; tTG, tissue transglutaminase.





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Endocrinology Section, Department of Medico-Surgical Sciences and Biotechnologies (C.V., M.G.S., S.C.D.D., M.C.), Department of Experimental Medicine (G.B., R.I., V.M., P.G.), and Gastroenterology Unit, Department of Internal Medicine and Medical Specialties (A.P.), "Sapienza" University of Rome, 00161 Rome, Italy; and Endocrinology Unit (L.G., M.C.), Azienda Unità Sanitaria Locale di Latina, 04100 Latina, Italy

**Objective:** Replacement $T_4$ dose in hypothyroid patients bearing both chronic autoimmune thyroiditis and atypical celiac disease (CD) has been analyzed.

**Design:** Replacement $T_4$ dose has been analyzed in 35 hypothyroid patients with Hashimoto's

**So a screening for (WRD) may be useful to improve therapeuticT4 effectiveness in patients with autoimmune thyroid disease**

$\mu g/kg \cdot d$; +49%; $P = 0.0002$) than in hypothyroid patients without CD.

**Conclusions:** Atypical CD increases the need for $T_4$. The effect was reversed by GFD or by increasing $T_4$ dose. Malabsorption of $T_4$ may provide the opportunity to detect CD that was overlooked until the patients were put under $T_4$ therapy. ***(J Clin Endocrinol Metab* 97: E0000–E0000, 2012)**

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# Serum *Helicobacter pylori* CagA antibody as a biomarker for gastric cancer in east-Asian countries

**Seiji Shiota**[1], **Osamu Matsunari**[1], **Masahide Watada**[1], and **Yoshio Yamaoka**[1,2,†]

[1] Department of Environmental & Preventative Medicine, Oita University Faculty of Medicine, Hasamamachi, Yufu-City, Oita, Japan

[2] Department of Medicine – Gastroenterology, Baylor College of Medicine & Michael E DeBakey Veterans Affairs Medical Center, Houston, TX, USA

## Abstract

**Aims—**In east-Asian countries, while almost all *Helicobacter pylori* strains possess the cytotokine-associated gene A (*CagA*) gene, serum CagA antibody is not detected in some infected subjects. We aimed to clarify the association between anti-CagA antibody and gastric cancer in east-Asian countries.

**Materials & methods**—We performed a meta-analysis of case–control studies with age- and

increased risk of developing gastric cancer.

**Conclusion—**Anti-CagA antibody can be used as a biomarker for gastric cancer even in east-Asian countries.

## Keywords

anti-CagA antibody; east Asia; gastric cancer; *Helicobacter pylori*

**The best-studied virulence factor of *H. pylori* is the cytotokine-associated gene A (CagA) protein.**

*Helicobacter pylori* (*H. pylori*) infection is now accepted as the major cause of chronic gastritis. Several epidemiological studies have shown that *H. pylori* infection is also linked to the severe gastritis-associated diseases, including peptic ulcer and gastric cancer [1]. In 1994, the International Agency for Research on Cancer categorized *H. pylori* infection as a group I carcinogen [2]. Although gastric cancer is one of the most common cancers, only a minority of individuals with *H. pylori* infection ever develop it. The prevalence of gastric cancer is approximately 3% in *H. pylori*-positive patients [3]. One possible reason for the

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# *Helicobacter pylori* CagA antibodies and thyroid function in latent autoimmune diabetes in adults

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*Alessandro P. Delitala and Giovanni M. Pes contributed equally to the work*

**The correlation between antibodies against CagA and TSH was significant as well as the correlation between anti-CagA antibodies and TPO Ab, as reported in Figures 1 and 2.**

**and GagA was 52.1% and 20.9% respectively. Antibodies against *H. pylori* were not associated with TPO Ab and TSH (rho = 0.067, *p* = 0.620 and rho = 0.156, *p* = 0.099, respectively). Antibodies against CagA showed a positive association with TSH and TPO Ab (respectively rho = 0.309, *p* = 0.036 and rho = 0.419, *p* = 0.037). Subjects with hypothyroidism (TSH ≥ 3.5 μU/ml) had an increased frequency of Ab anti CagA (*p* = 0.059).**

**CONCLUSIONS: The infection by *H. pylori* strains expressing CagA is associated with increased TPO Ab and TSH levels in LADA patients, suggesting a possible mechanism involved in thyroid autoimmunity and dysfunction of the gland. Further research is needed to test this hypothesis.**

*Key Words:*
Latent autoimmune diabetes in adults, CagA, Antibodies against thyroperoxidase, Thyrotropin.

## Introduction

Autoimmune thyroid disease (AITD) is characterized by the presence of circulating antibod-

*litica* and hepatitis virus C were found to be highly prevalent in patients with AITD[6-9], but a clear evidence is still lacking.

Helicobacter pylori (*H. pylori*) is a Gram-negative bacterium which colonizes the gastric mucosa and is widely accepted as a major cause of gastritis, gastric and duodenal ulcers[10-12]. A possible association between *H. pylori* with lymphoid tissue lymphoma and gastric cancer has also been proposed[13-17]. In addition, *H. pylori was* found to be linked also with extra-gastric manifestations such as autoimmune thrombocytopenic purpura[18], type 1 and type 2 diabetes mellitus[19-21], and a number of other conditions[22-24]. The relationship between AITD and *H. pylori* is controversial and conflicting results are reported in the literature.

Latent autoimmune diabetes in adults (LADA) is a type of autoimmune diabetes characterized by the presence of antibodies against glutamic acid decarboxylase 65 (GAD65 Ab) with a clinical picture very similar to type 2 diabetes at diagnosis. As other autoimmune diseases, LADA pa-

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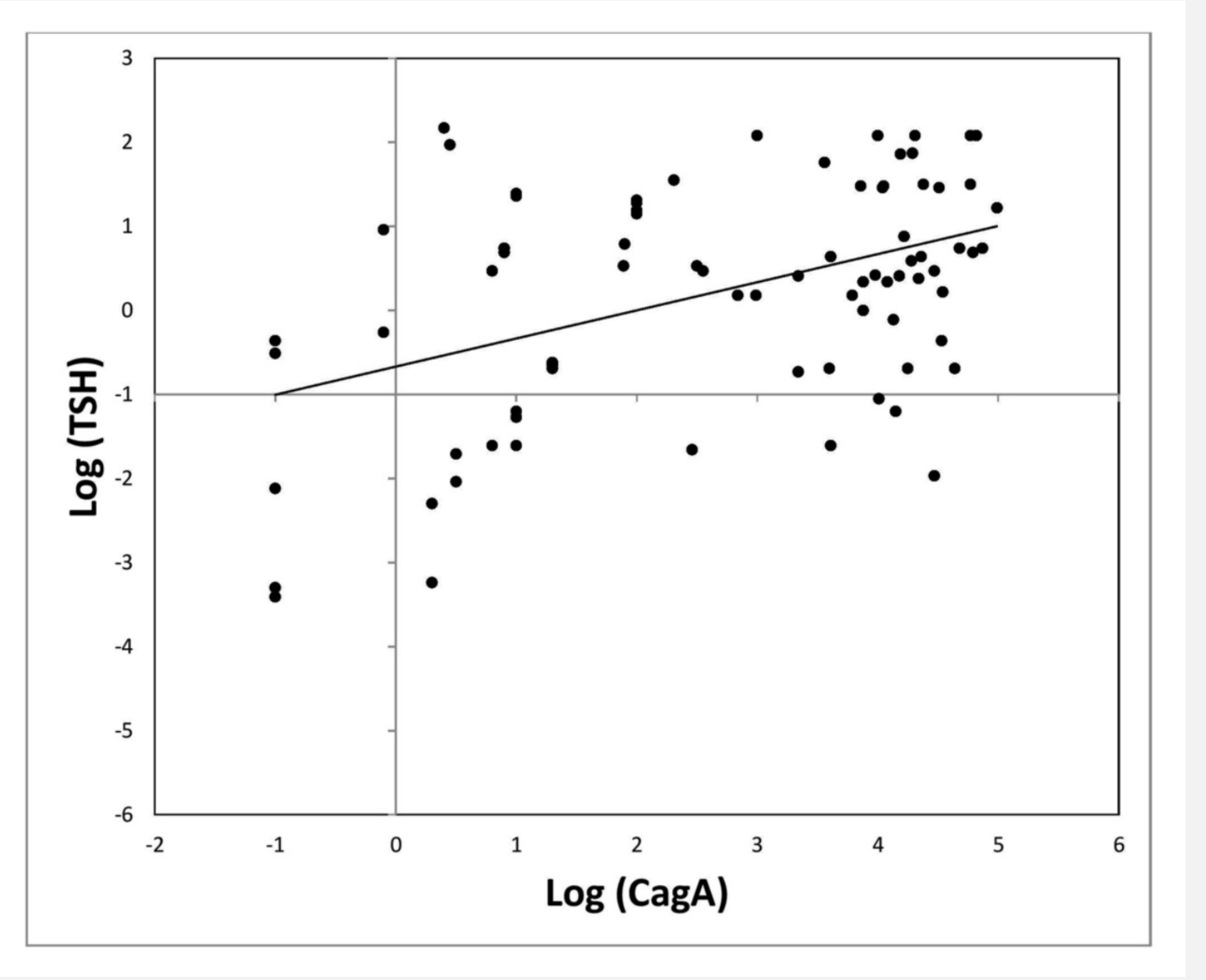



**Figure 1. Correlation between TSH and antibodies against CagA.**

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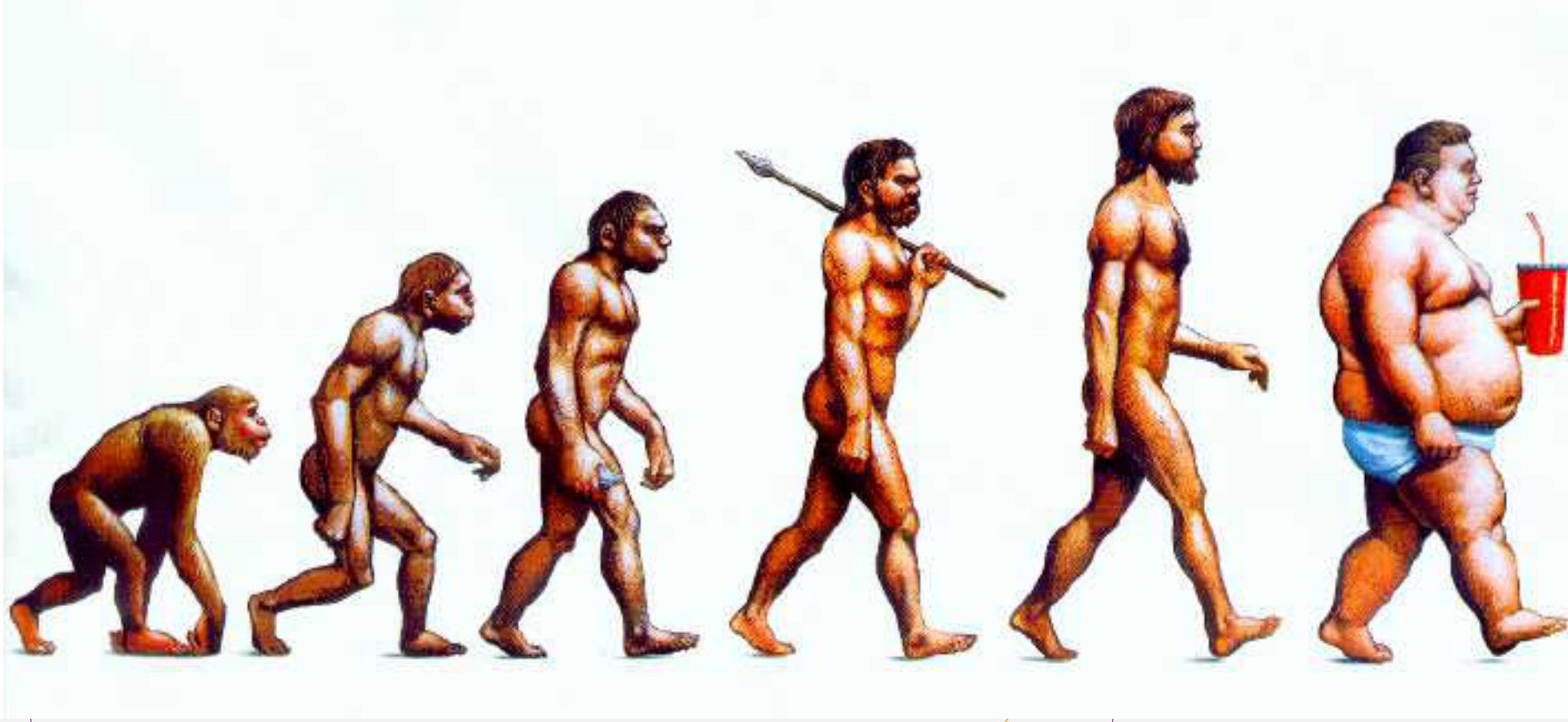
**In the present study, we showed that both TPO Ab and TSH levels were directly and significantly correlated with CagA Ab titer. Subgroup analyses also revealed that patients with hypothyroidism (defined as TSH ≥ 3.5 μU/ml) had an increased frequency of antibodies against CagA.**

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Adrenal

↓

Thyroid

↓

Sex Steroids



# Iodine

**Halogens are a group of elements in the periodic table, which include iodine, chlorine, bromine, fluorine and astatine. Molecules of thyroid hormones contain iodine in their structure.**

**The trouble is that other halogens, such as fluorine, chlorine and bromine have an ability to push iodine out of those molecules, making them dysfunctional and causing hypothyroidism.**



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## Chapter 32
## Clinical Approaches to Hormonal and Neuroendocrine Imbalances

- *Cellular Messaging, Parts I and II*
- *The Hypothalamus-Pituitary-Adrenal Axis*
- *Managing Insulin and Glucose Balance*
- *Perimenopause, Menopause, and Women's Health: The Dance of the Hormones, Part II*
- *Fibroids and Endometriosis*

**Goitrogens may block iodine utilization. Both soybeans and Brassica family of vegetables are goitrogens, which appear to reduce thyroid hormone output by blocking the activity of thyroid peroxidase, the enzyme responsible for adding iodine to the thyroid hormones.**

centered approach.

- Health is a state of positive vitality related to maintenance of a homeodynamic physiology that reflects a balance both between and among internal and external factors.
- Disease in the adult is often the result of a progressive loss of physiological, cognitive, emotional, and physical function and flexibility (that is, loss of organ reserve).

The antecedents of disease in an individual are dictated in part by the unique set of genetic characteristics

epigenetic influence on genetic expression in the offspring that can be passed on to subsequent generations.[1] This relationship ties genes and environment together in ways that go beyond simple Mendelian genetics.

The mediators released as a result of exposure to these triggers represent a broad array of intercellular communication agents. These can be large and protein-like in structure (e.g., insulin) or small (e.g., the sex hormones). Table 32.1 provides a list of representative intercellular communication mediators, their type, and their function.

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**While soy foods and Brassica family vegetables (turnips, cabbage, broccoli, cauliflower, Brussels sprouts, mustard greens, kale, kohlrabi, rutabaga) are the primary sources of goitrogens, they are also found in small amounts in peanuts, pine nuts, millet, peaches, strawberries, spinach, and cassava root.**

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**Both isoflavones and isothiocyanates appear to be heat-sensitive, and limited research suggests cooking, specifically boiling, lowers the availability of these substances. However, since boiling crucifers results in the loss not only of goitrogens but of important nutrients as well, patients for whom goitrogens may be problematic can be advised to briefly steam these vegetables and consume them in modest amounts.**

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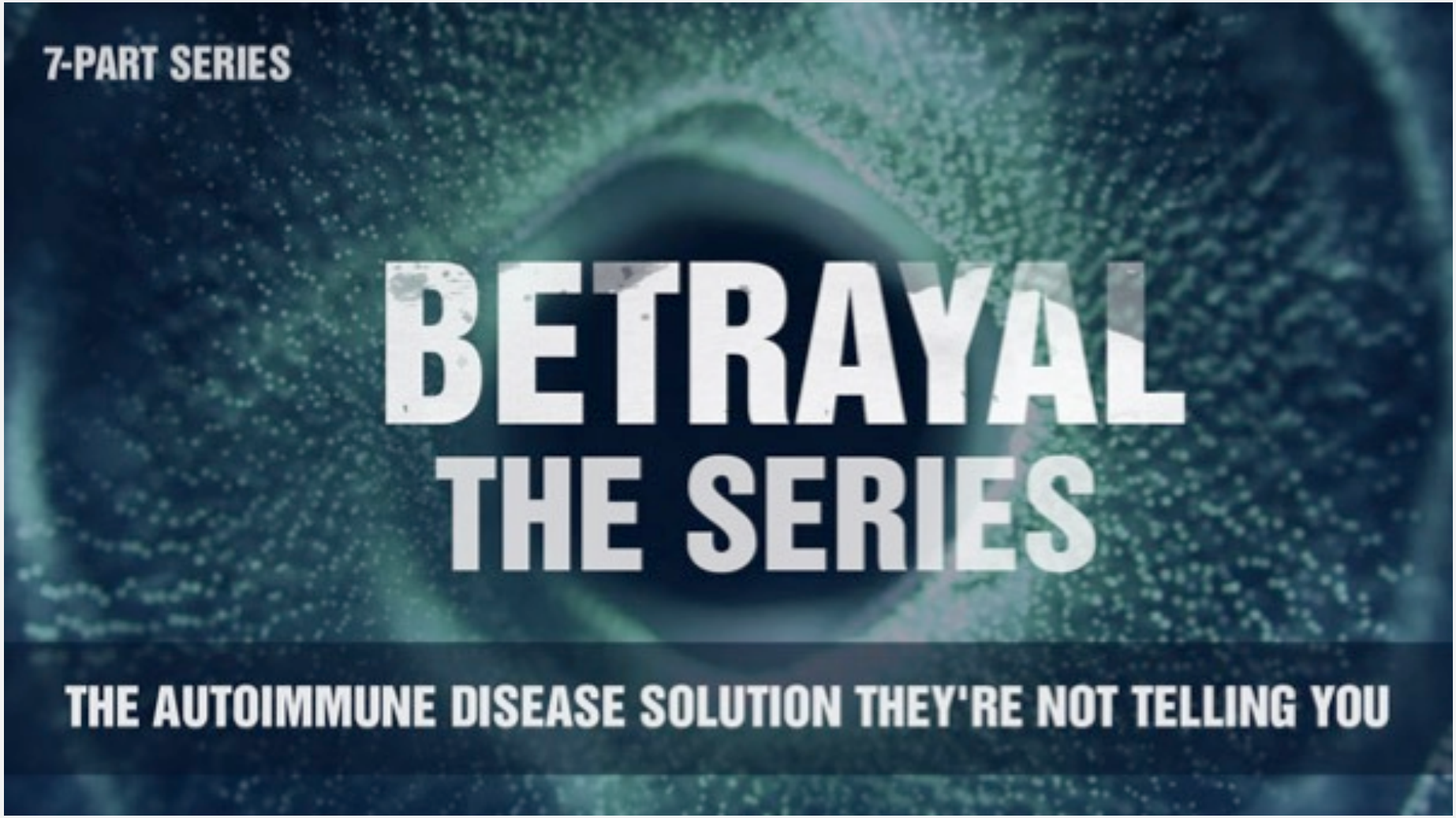
their function.

# Abdominal Swab

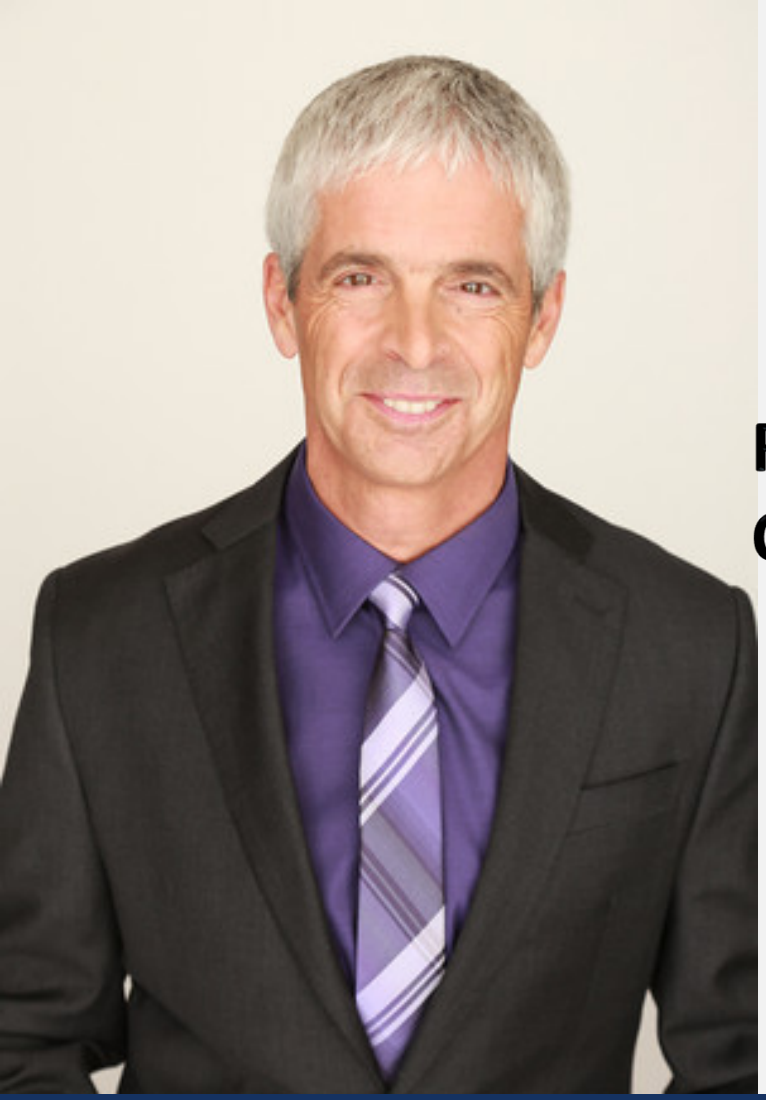
**Tincture of iodine is often found in emergency survival kits, used both to disinfect wounds and to sanitize surface water for drinking.**



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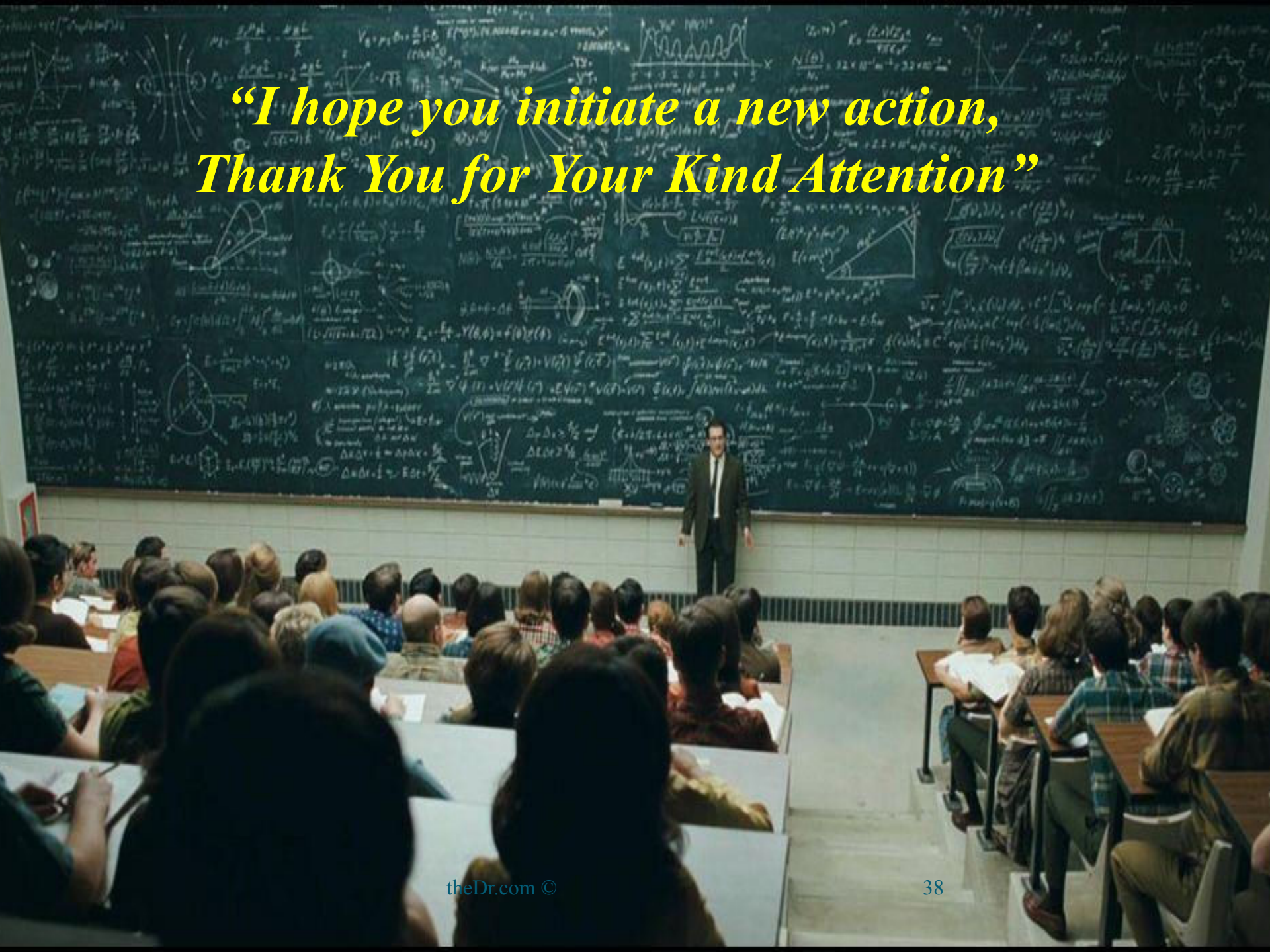
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