

Role of the Innate Immune System in the Pathogenesis of Gluten Sensitivity : Preliminary study

*A. Sapone, L. Imbrici, M. T. Giuliano, M. Cammarota,
M. De Rosa, M. Carteni, C. Tolone, A. Papparella, G.
Paolisso, V. Familiari, L. de Magistris, A Fasano*



Clinical Spectrum of Celiac Disease

The Celiac Iceberg



Genetic predisposition: DQ2 e/o DQ8
The others genes???



The Clinical Manifestations of Celiac Disease are More Heterogeneous Than Previously Appreciated

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS



Celiac Disease — How to Handle a Clinical Chameleon

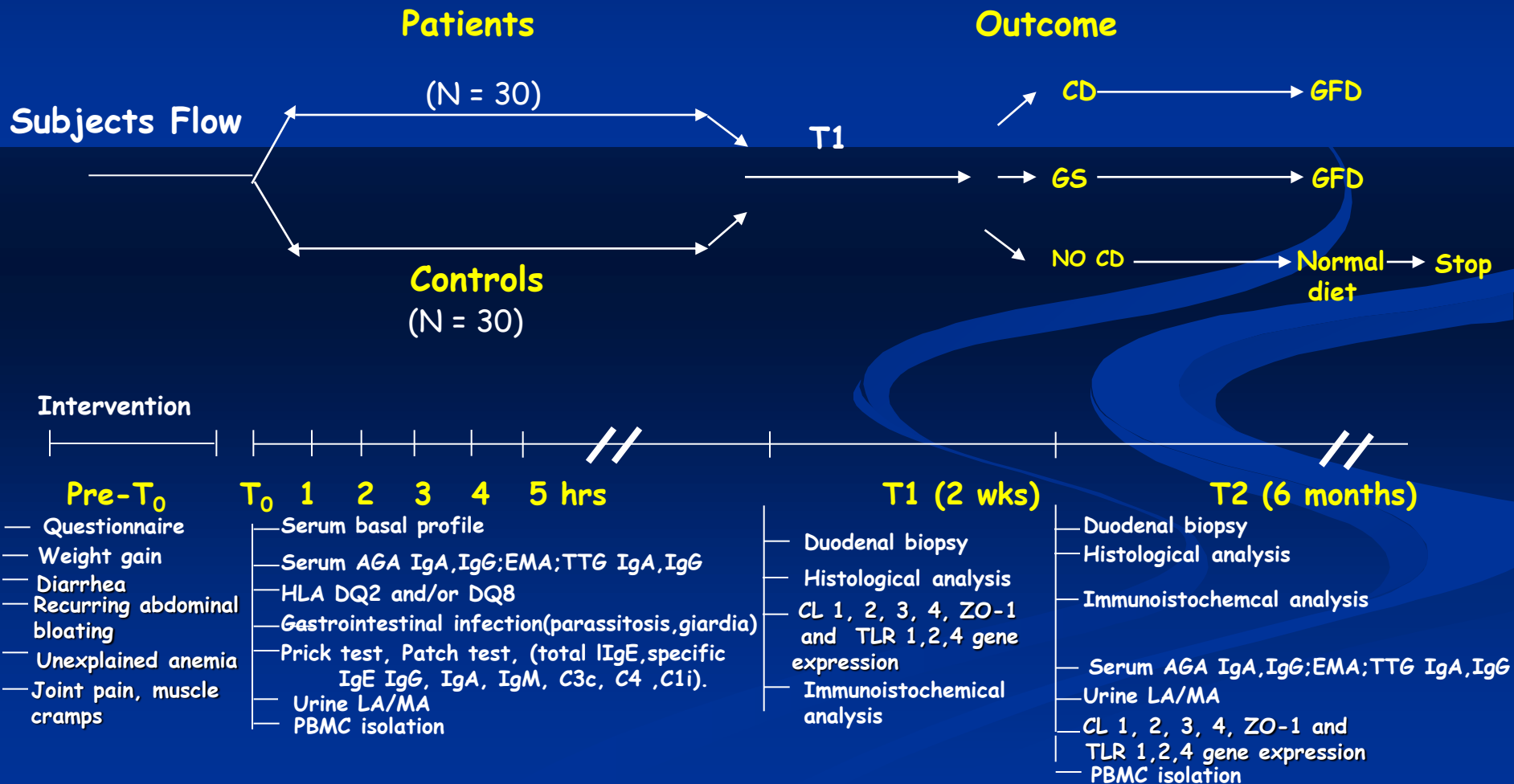
Alessio Fasano, M.D.

Celiac disease is an immune-mediated enteropathy triggered by the ingestion of gluten-containing grains (including wheat, rye, and barley) in genetically susceptible persons. The disease is associated

Epidemiologic studies conducted during the past decade, using specific and sensitive serologic tests, have revealed that celiac disease is one of the most common lifelong disorders in both Europe⁴



Flow Chart Gluten Sensitive Study



Results:

Percent positive

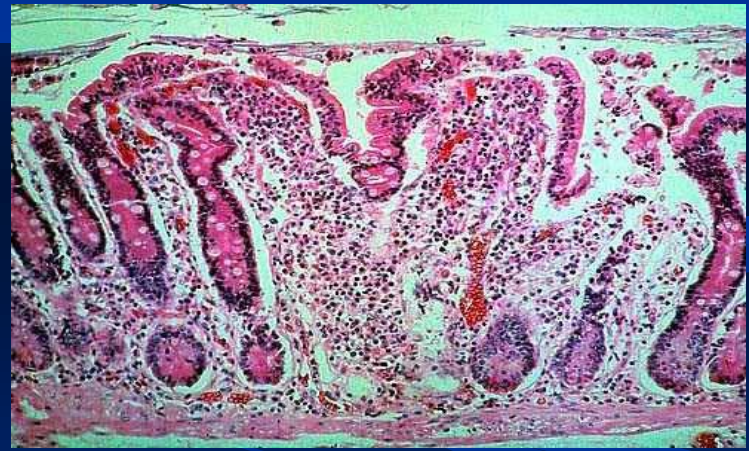
	Healthy	GS	Celiac	CD-GFD
AGA	0%	50%	100%	0%
EMA	0%	0%	100%	0%
tTG	0%	0%	100%	0%
HLA DQ2/DQ8	30%	50%	100%	100%
PRICK/ RAST/ PRIST test	0%	0%	20%	0%
LA/MA test	0%	0%	80%	0%

Results: Duodenal biopsy

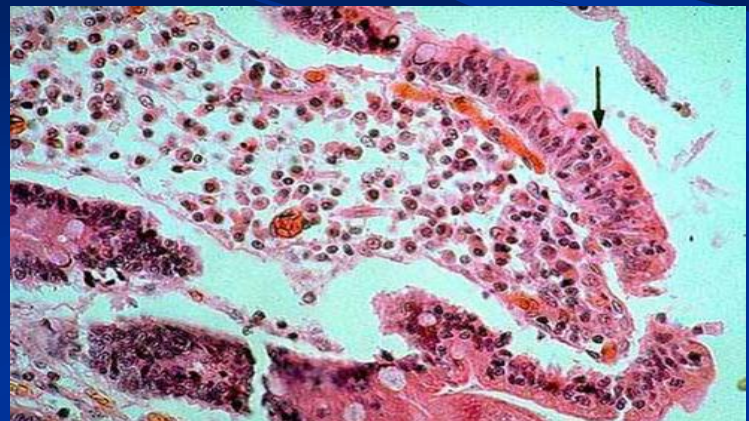
Normal histological appearance of the duodenum in healthy control



Typical intestinal damage in CD patient characterized by total villous atrophy, crypt hyperplasia with increased mitoses, an increased inflammatory infiltration of the lamina propria.



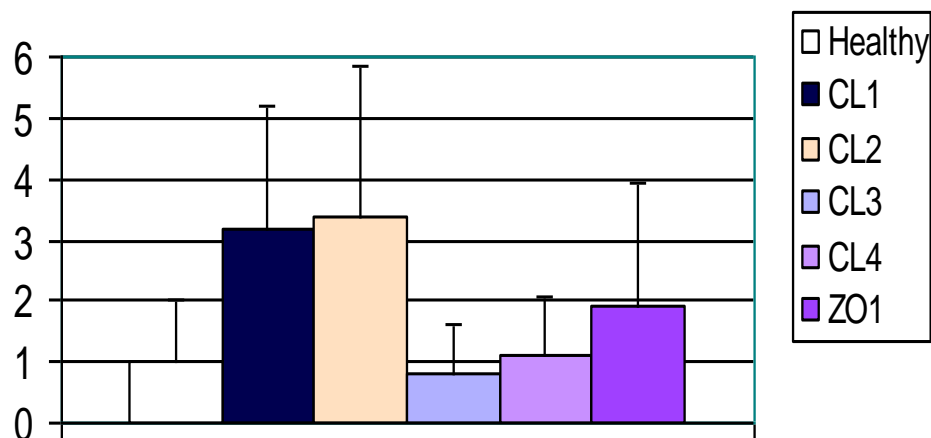
Non-specific duodenitis with increased number of lymphocytes in the lamina propria and an increase in transepithelial migration of lymphocytes (see arrow).



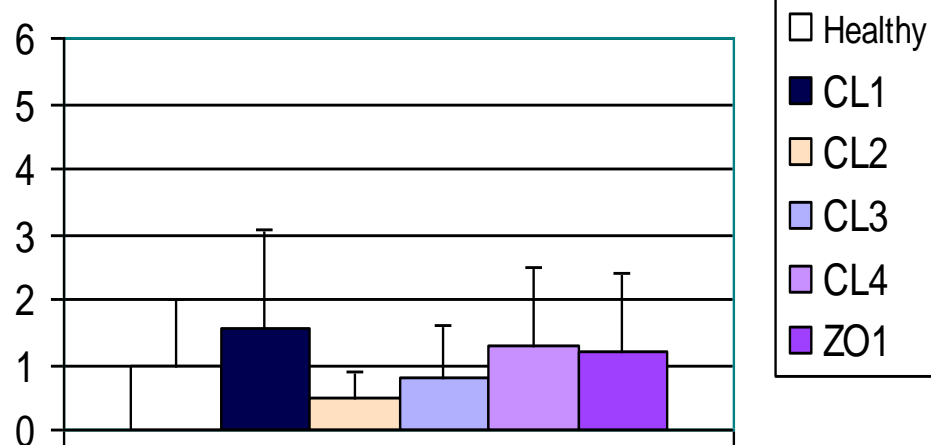
Results:

Intercellular TJ Protein Genes Expression in Active CD and After Remission Following GFD

Celiac Disease



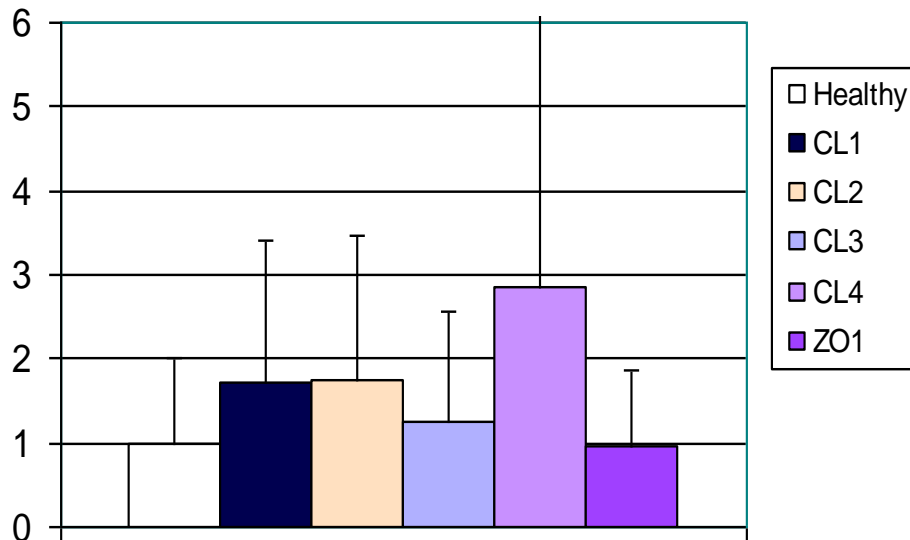
Celiac GFD



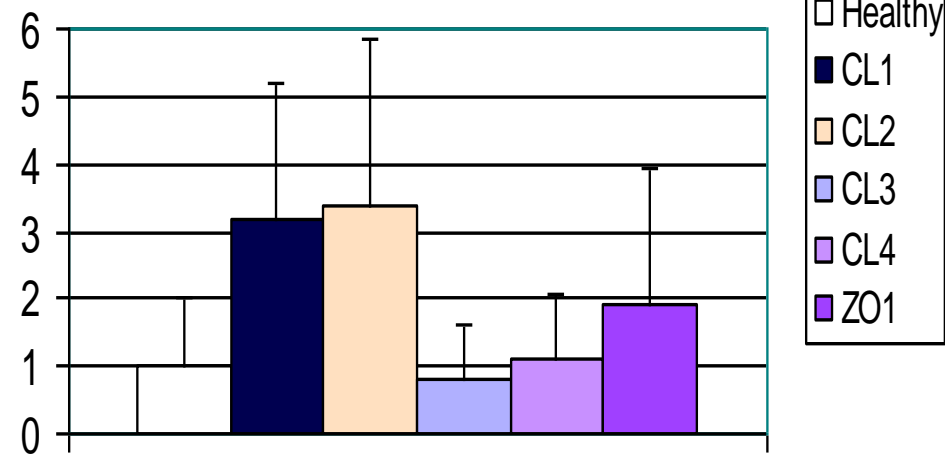
A significant over-expression of both Claudin (CL) CL1 and CL2 was observed in CD patients as compared to healthy controls, while no significant changes in CL3, CL4, and ZO-1 were detected. Remission of CD following implementation of a GFD reverted CL1 and CL2 over-expression to baseline values.

Results: Intercellular TJ Protein Genes Expression in GS Patients

Gluten Sensitive



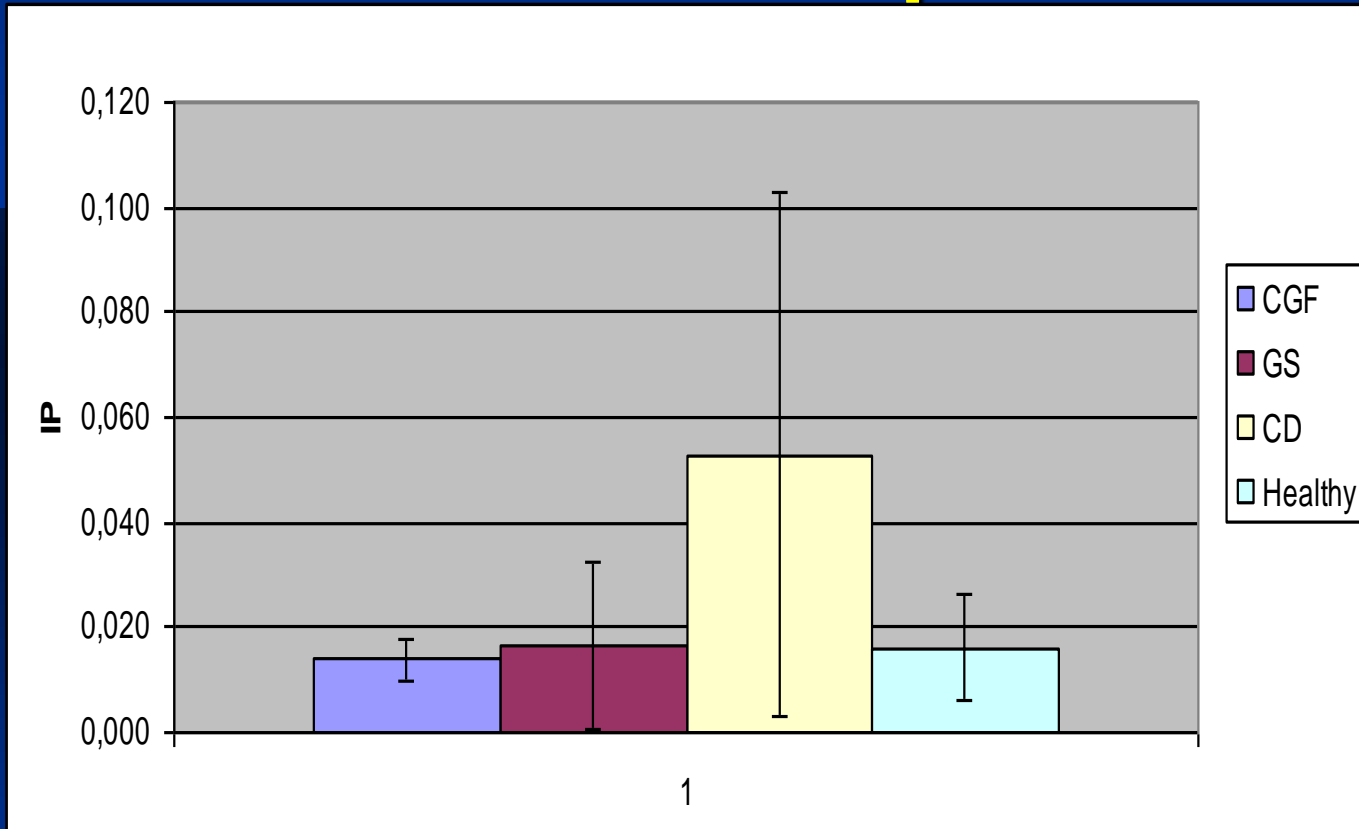
Celiac Disease



Expression of CL4 was increased three folds in GS subjects compared to both CD patients and healthy controls, while no changes in CL1, CL2, CL3, and ZO-1 expression were detected.

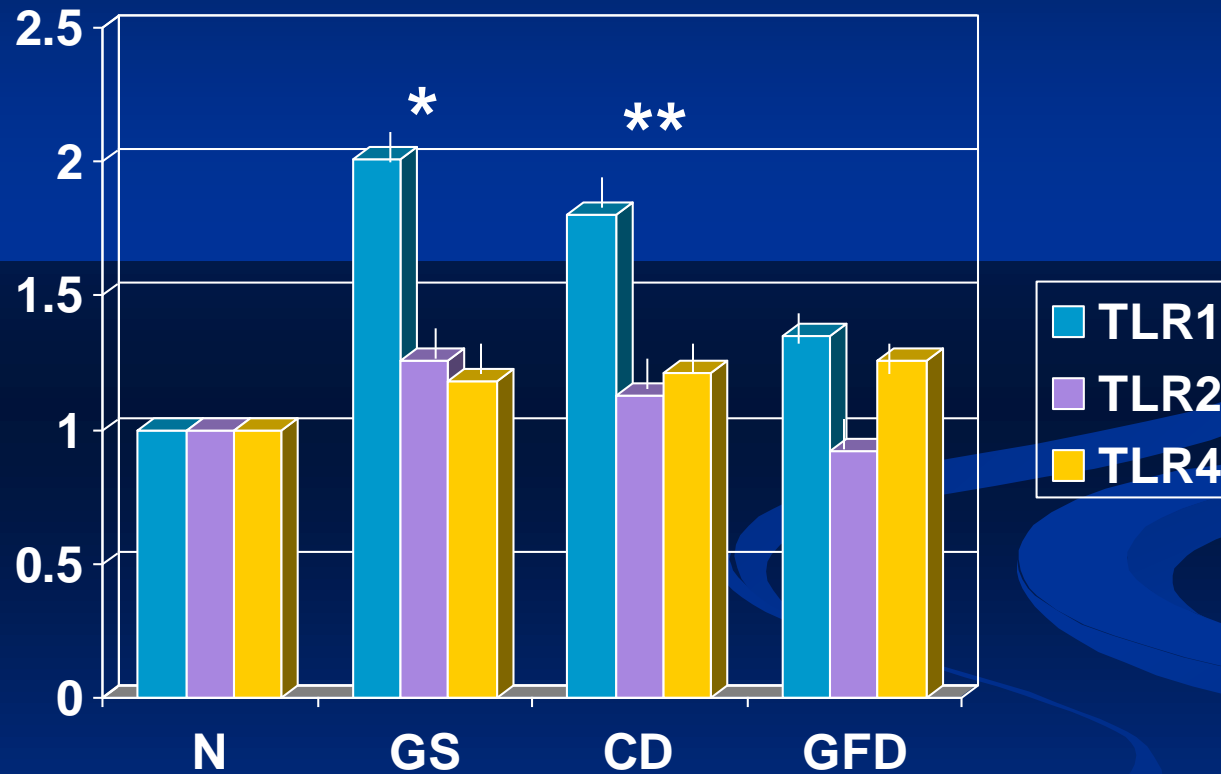
Results:

Change in Intestinal Permeability in GS and CD patients



In GS patients Intestinal Permeability (IP) (0.014 ± 0.015) was similar to that detected in healthy controls (0.019 ± 0.018). Conversely, in CD the increased expression of CL1 and CL2 was associated to an increase in IP (0.052 ± 0.048) that, however, did not reach statistical significance. In CD patients in remission, IP (0.014 ± 0.004) returned to normal levels.

Results: TLR Genes Txpession



* P = 0.0039 GS vs N

** P = 0.027 CD vs N

Conclusions:

- Compared to CD patients, GS subjects showed normal IP and CL1 and CL2 expression.
- Up-regulation of CL4 in GS patients did not influence IP.
- These results suggest that the pathogenesis of GS is different from that of CD and does not involve the loss of intestinal barrier function.
- The over expression of TLR 1 in CD and GS could suggest an important role of innate immune system in both conditions.
- **Gluten Sensitivity** appears to be a new chapter in the book of "Food intolerance" to be investigated.

