

# ADULT COELIAC DISEASE

F. Marmouz (1)

**SUMMARY:** Coeliac disease is an auto-immune inflammatory reaction characterized by a partial or total villi's atrophy of the proximal small intestine occurring after ingestion of gluten in genetically predisposed patients.

The classic form is much more frequent in children. Thereby there has been a misevaluation and improper treatment of coeliac disease in adults who suffer more from asymptomatic and atypical forms.

Currently the only effective treatment is a strict gluten free diet for life.

However recent researches brought a new light on the matter. Now oats as a causative factor is controversial. The introduction of some moderate intestinal lesions (pre-atrophic with intra-epithelial hyperlymphocytosis qualified as « weak enteropathies) in the definition of coeliac disease might be possible.

Moreover the way to diagnose has evolved as serological tests and markers are more used due to their efficiency.

**Key-words:** Adult - Coeliac - Disease - Gluten - Atrophy of the villi - Auto-immune disease.

**C**oeliac disease in adults is an enteropathic auto-immune condition caused by ingestion of gluten in genetically predisposed patients. It is characterized in its classic form by severe atrophy of the villi predominantly in the small intestine and is more marked proximally, which improves when wheat gluten is excluded from the diet and the equivalent prolamines of other implicated cereals (barley, rye, oats)

Two recent ideas modify this definition:

- oats as a causative factor is controversial
- moderate intestinal lesions, called pre-atrophic with intra-epithelial hyperlymphocytosis and qualified as "weak" enteropathies, can be included in the definition if they are decreasing when using gluten free diet.

Till recently considered as rare and affecting essentially children, the prevalence of Coeliac Disease has been reevaluated, especially in adults. It is an auto-immune disease, difficult to diagnose and improperly treated.

## EPIDEMIOLOGY

In France more than 150,000 people and in excess of 2 million Europeans are affected by Coeliac Disease. The majority are adults. The peak age of diagnosis of Coeliac Disease. In children is between 6 and 24 months of age, whilst in adults the peak is usually between 40

and 50 years of age. Twice as many females are diagnosed compared to males. Lastly the risk of developing the disease is multiplied by a factor of 10 when a family history of Coeliac Disease is present. Caucasians are more at risk than other races.

## PATHOPHYSIOLOGY AND IMMUNOLOGICAL MECHANISMS

Coeliac Disease is an auto-immune inflammatory reaction characterized by partial or total atrophy of the villi of the proximal small intestine occurring after ingestion of gluten in genetically predisposed patients. It is a digestive hypersensitivity with an inappropriate immune response of the mucosa. Up to 95 % of patients express a HLA-DQ2 molecule. The toxic cereals for these patients are wheat, barley, rye the gliadins soluble fractions of gluten and some fractions of them such as alpha-gliadin are toxic substances. Gliadin is modified by a tissue transglutaminase, then presented by cells to T lymphocytes of CD4 chorion, the origin of the inflammatory reaction producing cytokines (TNF-alpha, Interferon gamma...), anti-bodies (anti-gliadin, tissue, antitransglutaminase, anti-endomysium...) and an infiltration of the small intestine by intraepithelial lymphocytes type CD8.

## Symptoms are often minors or atypical

The classic form is rare and represents the iceberg of the adult Coeliac disease (less than 20 % of the cases). The main signs are digestive and general: diarrhea

(1) Immuno-allergologue - 1, rue Thiers - 95300 Pontoise - marmouz.farid@wanadoo.fr

(with steatorrhea), abdominal pains, weight loss (with malnutrition) and anaemia.

The biological anomalies are indirect signs of malabsorption in the small intestine :

- anaemia, iron, folates and even vitamin B12 and vitamin K deficiency;
- hypocalcemia, hypomagnesia, source of cramps and tetany;
- hypoprotidemia, hypoalbumina.

The asymptomatic or atypical forms are more frequently seen in adults.

These represent the invisible part of the iceberg :

- haematological : ferric anaemia, even isolated hypsideremia;
- rheumatological : demineralisation, arthralgies, fractures;
- neurological: peripheral neuropathy (lack of), epilepsy (and cerebral calcifications), ataxia (vitamin E deficiency?).

### ■ Migraine.

■ **Digestive:** simulating a functional colopathy, mouth ulcers, unexplained increase of transaminases, severe hepatopathy (rare).

■ **Gynecological:** infertility, amenorrhea, foetal hypotrophy, miscarriages.

These atypical forms must be looked for in at risk patients : linked to first degree (10%), patients with Coeliac Disease, type I diabetics (5 to 10 %).

Trisomie 21 (Mongolism), patients suffering from one or more auto-immune diseases (dermatitis herpetiformis, thyroid disease).

■ Many other **morbid associations** are possible :

- *Hematological:* IgA - deficiency, haemolytic anaemia, thrombopenic purpura.
- *Nephrological:* IgA - nephropathy.
- *Hepatic and digestive:* primary biliary cirrhosis, Crohn disease and colorectal bleeding...
- Lupus, Sjögren myasthenia, polymyositis, rheumatoid polyarthritis.
- Atopia, asthma, disease of farmer's lung or poultry breeders.

■ **There are two criteria for diagnosis (C.F.D):** serological and histological.

- The efficiency of gluten free diet is not now an obligatory criteria as serological tests are more effective.
- Serological markers are indicated in case of suspicion of Coeliac Disease, very useful in atypical or asymptomatic forms and for the follow up during the use of a gluten free diet.

➤ IgA Endomysial antibodies: sensitivity > 90 %, specificity > 95 %.

➤ Their positivity:

- IgA Antigliadin : sensitivity 90 %, specificity 85 %.
  - IgG Antigliadin : sensitivity 75 %, specificity 90 %.
- This test is only of
- interest if the IgA test is not positive (2 to 3 % of cases).
  - IgA Antitransglutaminase : sensitivity : > 90 %, specificity > 99 % (ELISA method).

If the sensitivity of these markers is high, further blood tests must be addressed to a reference laboratory to avoid "false negatives" for the endomysial antibodies.

A selective deficiency in IgA (2 to 3 % of cases) can lead to a "false negative" if we don't look for IgG antibodies.

A positive serology does not negate neither duodenal biopsy (fibroscopy), nor the start of a G.F.D. because of the possibility of false positives.

The histological criteria (duodenal biopsies by fibroscopy) are:

- Villous atrophy (generally total or subtotal).
- Increased epithelial lymphocytosis.
- Hyperplasia of the crypts.

## TREATMENT AND OUTCOME

The treatment rests solely on a G.F.D. for life, excluding all food containing wheat, barley or rye and any medication containing gluten. This constraining diet requires the patients to buy special products and rarely, supplements of iron, folate, calcium, vitamin D...

Even if clinical improvement is often rapid using G.F.D. (from a few days to a few weeks), villous response generally appears between six and twenty four months.

The advantage of G.F.D. is not only regression of symptoms but also the eventual prevention of complications such as:

- bone demineralization (50 % of cases);
- auto-immune disease (diabetes or thyroid disease);
- a rare invasive lymphoma which is six times more frequent in case of Coeliac Disease or other malign diseases.

The Coeliac Sprue is an enteropathy with villous atrophy characterized by the absence of any histological and clinical improvement despite a strict G.D.F.

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