PAEDIATRIC PATHWAY FOR COELIAC DISEASE

According to Mahatma Gandhi, "A correct diagnosis is three-fourths the remedy". Whilst this may be something of an overstatement, the IMPORTANCE of MEDICAL DIAGNOSIS is clear

BACKGROUND

It is recognised that an accurate and timely diagnosis provides an individual with the best opportunity for a positive health outcome.[1] In contrast, a diagnostic error may result in the individual being denied prompt, effective treatment or even being offered inappropriate and potentially dangerous therapies. Diagnosis is of particular importance in a condition like coeliac disease, which is life-long; has profound health effects; and for which treatment has huge lifestyle implications. The positive benefits of an early and correct diagnosis are especially important for children with coeliac disease in order to optimise growth and development. In contrast, the effects of an incorrect diagnosis are keenly felt in this group, as they may experience longstanding unpleasant symptoms or receive inappropriate and ineffective treatment

The diagnosis of coeliac disease has evolved over the decades since a gluten-sensitive enteropathy was first recognised by Dutch Paediatrician, William Dicke in 1950.[2] Key to this evolution has been the development of increasingly accurate blood tests to identify the immunological features of coeliac disease. The original anti-gliaden antibody tests which had relatively poor accuracy have been superseded by far more sophisticated and reliable tests, including the tissue transglutaminase and endomysial antibody tests.

As well as improvements in blood tests, there has been an increased awareness and understanding that coeliac disease is a complex, immune-mediated disorder with effects on many bodily organs and functions, rather than being a disease which only affects the intestine. This recognition has brought into focus the question as to whether a diagnosis which rests solely on intestinal biopsy is accurate, appropriate and fit for purpose for all individuals with coeliac disease, some of whom may have few if any, gastroenterological symptoms.

Furthermore, a biopsy-based diagnosis requires the individual to undergo an endoscopy. Although endoscopy is generally extremely safe and straightforward, it is an invasive procedure which is not wholly without risk or inconvenience to the individual. This is of special note for children who usually undergo endoscopy as a hospital inpatient under general anaesthesia. Endoscopy is also a relatively costly procedure for which there may be limitations in availability and accessibility related to health service constraints.

The status of intestinal biopsy as the "Gold Standard" (best and most accurate) diagnostic test for coeliac disease has also been questioned. Although it remains an important tool in diagnosis, the correct diagnosis may be hampered by poor biopsy technique; insufficient biopsies; and variations in reporting of biopsy findings.[3] It is also recognised that coeliac disease may cause patchy injury to the intestine, which may result in missed diagnoses if biopsies are not taken from the affected areas.[4]

Hence the publication by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) in 2012 of guidelines advocating biopsy-free diagnosis of coeliac disease in children was met with great interest.[5] These guidelines suggested that, for children with typical symptoms of coeliac disease, a diagnosis could be made without the need for intestinal biopsy if the child had strongly positive coeliac blood tests (on two separate blood samples) and compatible genetic (HLA) tests. The guidelines were subsequently revised to indicate that HLA testing is not required, and that biopsy-free diagnosis can also be considered for asymptomatic children with strongly positive blood results.[6]

This paper raised the exciting prospect of introducing a biopsy-free diagnosis of coeliac disease for New Zealand children. Estimates from Auckland data at the time suggested that around 50% of children might be able to be diagnosed without endoscopy if these guidelines were adopted. However, it was important to consider whether the introduction of biopsy-free diagnosis was a safe and reliable undertaking for our children. The ESPGHAN paper had been published by a group of professionals in Europe and did not include any data from Australasia. Although there was no reason to suspect that coeliac disease is a fundamentally different disease in New Zealand, previous research had raised concerns that the diagnostic accuracy of our local laboratory tests might not be sufficient to allow the safe introduction of biopsy-free diagnosis.[7]

To investigate this issue further, between 2013 and 2014 the Paediatric Gastroenterology team at Starship Hospital carried out a study in the Auckland area into the potential accuracy of biopsy-free diagnosis. One hundred patients undergoing endoscopy for the possible coeliac disease had blood tests performed as per the ESPGHAN guidelines. This study confirmed that the guidelines held true in our population. Furthermore, it demonstrated that up to 60% of patients could avoid an endoscopy if biopsy-free diagnosis was adopted.[8]

In 2018 a diagnostic pathway was introduced in the Auckland

PAEDIATRIC PATHWAY FOR COELIAC DISEASE

BACKGROUND *(cont)*

area which incorporated biopsy-free diagnosis for children referred to Paediatric Gastroenterology services with possible coeliac disease. Any child with strongly positive antibody tests as per ESPGHAN guidelines is considered for a biopsy-free diagnosis. A second confirmatory blood test is requested. If this second result is similarly positive, the family is offered a phone consultation to discuss a biopsy-free diagnosis and the introduction of gluten-free diet. Since the instigation of this diagnostic pathway, nearly 70% of all children diagnosed with coeliac disease in the Auckland region have received a biopsy-free diagnosis.

The benefits to children with coeliac disease of a quicker, less invasive diagnostic process are clear. No parent of a child eligible for biopsy-free diagnosis has yet requested a confirmatory endoscopy, indicating that this is an acceptable option to families. Furthermore, there have been positive benefits to the wider group of patients requiring gastroenterology care, as the introduction of biopsy-free diagnosis has resulted in a reduction in waiting times for endoscopy (including for those children who still require histological confirmation of coeliac disease).

Although biopsy-free diagnosis has been adopted successfully in the Auckland area, it has yet to be rolled out nationwide. This is an important next step to consider, in order to provide effective, timely and equitable care for all of our tamariki. However, any nationwide roll-out needs to be carried out with due care and attention. The Auckland study investigated the diagnostic accuracy of tests used in local laboratories but did not look more widely at tests used around the country. Although there is local expertise in the use and interpretation of these tests, not all laboratories offer precisely the same type and range of tests. Discussions are ongoing to explore whether a consistent testing approach could be achieved across laboratories to permit consideration of biopsy-free diagnosis for children with coeliac disease across New Zealand.

Article provided Dr Jonathon Bishop.

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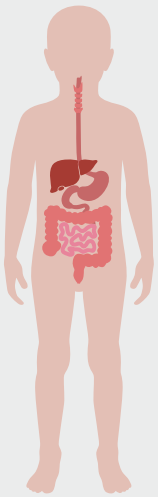
Symptoms in children

When gluten containing food is added to the infant diet.



- IRRITABILITY
- POORLY CALCIFIED TEETH
- NAUSEA AND VOMITING
- POOR WEIGHT GAIN/ POOR GROWTH/
- WEIGHT LOSS IN OLDER CHILDREN
- IRRITABLE BOWEL SYMPTOMS/ DIARRHOEA/ LARGE, BULKY, FOUL STOOLS/ CHRONIC CONSTIPATION
- CHRONIC ANAEMIA

WHO TO TEST?

Symptomatic paediatric patients with:

- A bloated stomach, diarrhoea and/or constipation
- General tummy upsets and/or vomiting
- Tiredness or lack of stamina
- Anaemia
- Poor growth or physical development
- Failure to thrive, difficulty concentrating at home or at school
- Poorly calcified teeth.

Note: do not exclude gluten from a child's diet until they have received a diagnosis by a healthcare professional.

Steps to diagnosis in children

WHO TO TEST

Does their diet contain adequate gluten?
Serology results will be unreliable if already on a gluten-free diet

Yes

No

Offer coeliac serology testing[1]
- IgA tTG
- Total IgA

Willing?

Suggest gluten challenge
2-3 slices of bread or equivalent daily for 4 weeks

Not willing?

Consider HLA DQ2/ DQ8 testing
- Negative test rules out coeliac disease
- Positive test *does not* confirm coeliac disease
- Offer review if gluten reintroduced

IgA tTG negative

IgA tTG positive

Low total IgA <0.5g/l

Normal total IgA

IgA tTG >10x ULN

IgA tTG >10x ULN[2]

Request IgG-based tests (tTG or DGP)

Positive Ig-G based test

No serological evidence of coeliac disease- look for another cause of the child's symptoms

Second serological test – EMA +/- IgA tTG

Negative Ig-G based test

EMA positive (+ IgA TTG positive, if tested)[2]

Coeliac disease diagnosis
- Refer to local paediatric/ paediatric gastroenterology service
- Refer to dietitian and provide patient with information about Coeliac New Zealand

Key

1. Testing offered may differ depending on local laboratory protocols.
1. May require diagnostic endoscopy.
2. May qualify for biopsy-free diagnosis but dependent upon decision making at paediatric level.