Coeliac Disease

Blood tests in investigation of coeliac disease

INTRODUCTION

Coeliac disease (CD) is an immune mediated systemic disorder with prominent enteropathic features triggered by exposure to the gluten (storage protein and related prolamine) fraction of wheat, rye and barley cereals, as well as some oat cultivars. There is a strong genetic component, in association with the HLA alleles HLA-DQ2 and HLA-DQ8. Most patients report a combination of symptoms including abdominal bloating, flatulence, abdominal cramps or discomfort, and altered bowel habit. A minority of patients have 'silent coeliac disease' with no intestinal symptoms. 'Latent coeliac disease' refers to patients who may develop CD in the future or have had CD in the past, but have a normal small bowel biopsy on a gluten-inclusive diet at the time of investigation. The symptoms and bowel inflammation of CD may be mitigated by adopting a gluten-free diet.

THE DIAGNOSTIC APPROACH TO COELIAC DISEASE

The diagnosis of suspected CD involves serological testing for antibodies, and upper intestinal endoscopy with histological examination of a small bowel biopsy for confirmation in most cases. Endoscopy with biopsy findings confirms serological results and may exclude other causes of gastrointestinal pathology. The characteristic histology of CD shows intestinal villous atrophy, crypt hyperplasia and an intra-epithelial lymphocytosis.

Antibody measurement in investigation

Serological investigation of CD involves the detection of antibodies to gliadin (deamidated gliadin protein or DPG) and auto-antibodies to the antigen tissue transglutaminase. Thus, relevant assays are measurement of anti-gliadin antibodies and anti-tissue transglutaminase antibodies. In CD measurement of antibodies of IgA isotype provides optimal sensitivity and specificity (in contrast to most autoimmune disorders in which the antibodies tested for are of IgM or IgG isotype). IgG anti-gliadin testing is useful in infants and in patients with IgA deficiency. Antibody measurement is useful both diagnostically and also to monitor compliance with a gluten-free diet.

In general CD serology has both sensitivity and specificity of 95-98% for the diagnosis of CD. Factors that can reduce the sensitivity of antibody measurement to consider include early childhood, IgA deficiency, inadequate dietary gluten intake prior to testing and immunosuppressive medication.

Coeliac disease genotyping

CD is associated with the MHC proteins HLA-DQ2/DQ8. Because negative HLA-DQ2/ DQ8 status means CD is unlikely, coeliac genotype assessment may be useful when there are equivocal serological or biopsy results, or when a patient is on a gluten-free diet and does not wish to undergo a gluten challenge. However a positive HLA-DQ2/DQ8 status is not diagnostic as these are permissive genetic factors only and approximately 25-30% of the Australian population are HLA-DQ2/DQ8 positive, whereas only 1-2% of the population have CD. Thus, coeliac genotyping is useful for its negative predictive value, but it has minimal positive predictive value. Possible indications for measurement of a coeliac genotype include: equivocal or indeterminate antibody test results or small bowel biopsy result; to attempt exclusion of CD in a patient already on a gluten-free diet and unwilling to undergo a dietary gluten challenge; and to increase the diagnostic certainty in a child with a high clinical suspicion of CD, with positive antibody tests, and in whom an endoscopy and small bowel biopsy is not being performed.

IGA DEFICIENCY AND COELIAC DISEASE

Patients with total IgA deficiency are at an increased risk of CD, but may have negative tests for IgA anti-gliadin, IgA anti-endomysial and IgA tissue transglutaminase antibodies. In this population, measurement of IgG antibodies antibody is necessary, for example, IgG gliadin antibody.

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COELIAC DISEASE IN CHILDHOOD

Younger children of less than two years may have normal total IgA levels, but the immature immune system may not mount brisk IgA specific responses. Therefore, in younger children an IgG gliadin antibody may be measured in addition to testing for IgA tissue transglutaminase antibodies.

THE ROLE OF COELIAC SEROLOGY IN ASSOCIATED DISEASES

CD is associated with a number of autoimmune disorders including type 1 diabetes mellitus and autoimmune thyroid disease, as well as being associated with genetic disorders including Down syndrome and Turner syndrome. In some patients with osteoporosis or infertility, CD may be a contributing factor. Dermatitis herpetiformis is strongly associated with CD.

INDICATIONS FOR TESTING

Common indications for ordering coeliac antibodies:

- Childhood failure to thrive
- Chronic abdominal pain, bloating, flatulence, diarrhoea, recurrent apthous stomatitis
- Investigation of unexplained iron or folate deficiency
- Suspected dermatitis herpetiformis

Consider screening for coeliac antibodies in asymptomatic individuals with:

- Osteoporosis
- Type 1 diabetes mellitus
- Autoimmune thyroiditis
- Autoimmune hepatitis
- Down syndrome, Turner syndrome, Williams syndrome
- Other immunological associations and associated diseases

Diseases or associations with which CD is more common:

- 1st degree relative with CD
- Dermatitis herpetiformis
- IgA deficiency
- Down syndrome
- Turner syndrome
- Autoimmune thyroid disease
- Type 1 diabetes mellitus
- Polyglandular autoimmune syndrome
- Osteoporosis
- Infertility

PATIENT PREPARATION

Please ensure the patient maintains a gluten-inclusive diet for optimally 12 weeks prior to measurement of coeliac antibodies as some patients with CD may not develop an antibody (or mucosal response) in shorter periods.

HOW TO ORDER

Please request 'coeliac serology' on a standard Tasmanian Medical Laboratories request form. This generates a result for anti-tissue transglutaminase IgA antibodies and anti-gliadin IgG antibodies. To request assessment of HLA DQ2/DQ8 status please simply request 'coeliac genotype'.

TURNAROUND TIME

Coeliac serology results are normally available within 3 working days.

Coeliac genotype results are usually available within 1 week.

COST

Testing is bulk-billed subject to Medicare guidelines and criteria. If Medicare guidelines and criteria aren't met, an out-of-pocket fee may apply.

FURTHER INFORMATION

For further information please call
Hobart **(03) 6108 9900** or Launceston **(03) 6711 2000**

Dr David Heyworth-Smith
FRCPA FRACP
Consultant Clinical Immunologist
Immunology & Microbiology Department

Dr Paul Campbell
MB ChB, BSc (Hons), PhD (Oxford), FRCPA
Immunopathologist, Immunology

Ms Marie Hetherington
Chief Scientist, Immunology

Specialist Diagnostic Services Pty Ltd (ABN 84 007 190 043) t/a Tasmanian Medical Laboratories PUB/MR/1425, v1 (Apr-17)