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PATHOLOGY *focus*

Medical Newsletter

Season's greetings

and Happy New Year!

Thank you from the team at Clinical Labs

As 2025 draws to a close, we extend our heartfelt thanks for your continued partnership and trust in Clinical Labs. It has been a privilege to support you and your patients throughout another year of delivering excellence in pathology diagnostics.

We hope you've found value in this year's editions of *Pathology Focus*, featuring articles such as 'Annual Blood Tests for Men,' 'Optimising Cardiac Care,' and 'RSV Under the Microscope.' Looking ahead to 2026, we're excited to continue sharing insightful content from the world of pathology.

We wish you and your team a joyful festive season filled with rest and meaningful time with loved ones. From all of us at Clinical Labs - thank you, and here's to a healthy and successful New Year!

Genetic Susceptibility in Coeliac Disease and the Clinical Role of HLA Genotyping

By Associate Professor Mirette Saad

Coeliac disease (CD), also known as gluten-sensitive enteropathy, is a chronic autoimmune disease resulting from the inflammatory response to dietary gluten found in wheat, barley and rye in genetically predisposed patients. This article focuses on HLA typing in CD.

Epidemiology

Coeliac disease affects approximately 1% of the global population, and approximately 1 in 70 Australians have CD, with females being more commonly affected. Despite the rise in the prevalence and incidence of CD over time, only 20% of patients are diagnosed. Many patients remain undiagnosed or experience significant delays in diagnosis.

Clinical Presentation and Diagnostic Workup

CD diagnosis for patients on a gluten-containing diet is supported by a positive tissue transglutaminase serologic test but, in general, should be confirmed by a small bowel biopsy (gold standard diagnostic workup) showing the characteristic histology associated with CD.

> *NICE guidelines recommend testing for CD in patients presenting with classical and non-classical presentations, including chronic fatigue.*

Clinical manifestations of CD vary greatly according to age group. Diarrhoea and malabsorption are classic manifestations of CD; however, both children and adults can be paucisymptomatic and present extra-intestinal manifestations and systemic complications (Table 1). The National Institute for Health and Care Excellence (NICE) guidelines recommend testing for CD in patients presenting with classical and non-classical presentations, including chronic fatigue. An association between CD and autoimmune disorders and family history has been well documented (Table 1).

Table 1: Classical and Non-Classical Presentations and Indications for CD Testing

Classical	Non-Classical
• Bloating or abdominal distension; chronic diarrhoea or constipation, or abdominal pain and vomiting • Positive family history of first-degree relatives	• In childhood: developmental delay, failure to thrive and neurologic symptoms • In adulthood: sudden or unexpected weight loss • History of clinical autoimmune disease (such as type 1 diabetes mellitus, autoimmune thyroid disease, Sjögren's syndrome, IBD and multiple sclerosis) • History of iron deficiency anaemia, folate, vitamin D, vitamin K and calcium deficiency • History of bone disease such as osteoporosis and arthritis in adults • History of Trisomy 21 (Down syndrome) and Turner syndrome • Patients with chronic fatigue, weakness or hair loss

Genetic Disposition of CD

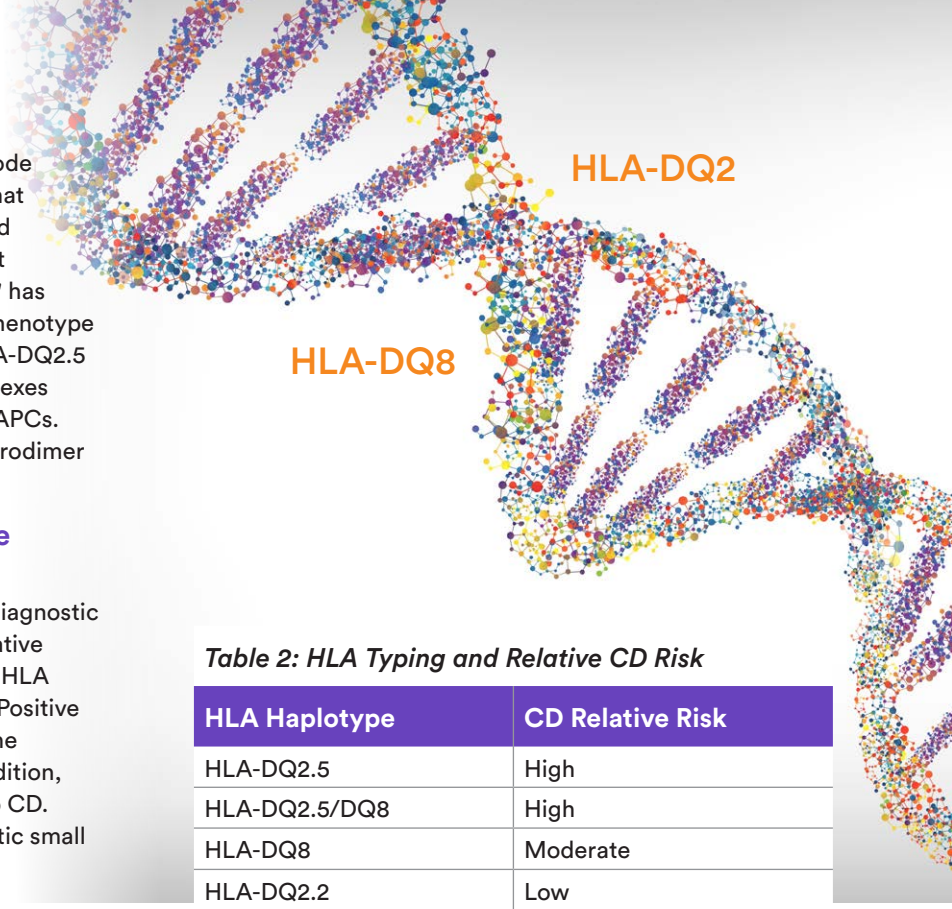
The main determinants for genetic susceptibility are the human leukocyte antigen (HLA) class II genes, particularly HLA-DQA1 and HLA-DQB1 genes encoding for HLA-DQ2 and HLA-DQ8 molecules, which are carried by almost all affected patients.

HLA susceptibility sets of alleles are expressed in a co-dominant manner. One set of alleles is inherited from each parent.

Approximately 90% of CD patients carry the heterodimer HLA-DQ2.5, leaving only a small proportion of patients with lower-risk heterodimers (HLA-DQ8 or HLA-DQ2.2).

HLA "Gene-Dose Effect" and CD Relative Risk

HLA genotyping is considered a solid support in the diagnostic algorithm of CD. **Unlike CD serology and intestinal histology, genotyping is a once-only test that is not reliant on gluten consumption for accuracy**.



Both haplotypes, HLA-DQ2 and HLA-DQ8, encode molecules on antigen-presenting cells (APCs) that orchestrate the immune response to deamidated gluten, playing a crucial role in the development and pathogenesis of CD. The "gene dose effect" has implications on CD development and disease phenotype (Table 2). Compared to other heterodimers, HLA-DQ2.5 has the potential to bind and form strong complexes with the immune-dominant gluten peptides on APCs. Therefore, individuals with the HLA-DQ2.5 heterodimer have a higher risk of developing CD (Table 2).

Recommendations for the Appropriate Clinical Use of HLA Typing in CD

The main utility of HLA typing is to assist with diagnostic risk stratification of CD. Due to a very high negative predictive value (NPV), a negative result for the HLA susceptibility genotypes virtually excludes CD. Positive results indicate CD risk, but it cannot confirm the diagnosis. Genetics alone do not cause the condition, as many people with these genes never develop CD. Supportive evidence with serology and diagnostic small intestinal biopsy is required.

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Table 2: HLA Typing and Relative CD Risk

HLA Haplotype	CD Relative Risk
HLA-DQ2.5	High
HLA-DQ2.5/DQ8	High
HLA-DQ8	Moderate
HLA-DQ2.2	Low
HLA-DQA1*05	Very Low
Negative HLA-DQ2 and HLA-DQ8	May exclude a diagnosis of CD (likelihood of CD <1%)

References and further reading

- NICE Clinical Guideline. 2015 https://www.nice.org.uk/guidance/ng20/resources/coeliac-disease-recognition-assessment-and-management-pdf-1837325178565
- Tye-Din *et al.* 2015

How to Order HLA genotyping for CD with Clinical Labs

What to write on the request form: Complete the Clinical Labs general pathology request form, requesting HLA genotyping for CD, DQ2/DQ8 or Coeliac disease genotypes.

Clinical notes recommendation: Include family history and associated symptoms or conditions.

Specimens required: EDTA tube

Test cost: Bulk-billed, subject to Medicare eligibility criteria. See MBS Item 71151 at mbsonline.gov.au.

Turnaround time: 7-10 business days from sample receipt in the lab.

Supplementary tests: Coeliac serology, nutritional status, iron studies.

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Associate Professor Mirette Saad is an RCPA Consultant Chemical Pathologist and the National Director of Molecular Genetics at Australian Clinical Labs. She has a Fellowship with Honours in Chemical and Molecular Pathology, with a Microbiology sub-speciality, from overseas. A/P Saad received her NHMRC-sponsored PhD degree in Cancer Genetics from Melbourne University and Peter MacCallum Cancer Institute. Along with her teaching and research roles, A/P Saad is a registered medical practitioner with AHPRA, a Chemical Pathology Fellow (FRCPA) at the RCPA and a Member of the AACB by examination. She is Chair of the RCPA Chemical Pathology Advisory Committee, a Member of the RCPA Genetic Advisory Committee and Chair of the Precision Medicine Services at Australian Clinical Labs.

Allergen-Specific IgE Testing: A guide for clinicians

Listen to the patient, they'll tell you the diagnosis.

By Associate Professor Louise Smyth

Allergy is clinically, economically and socially important, affecting approximately 30% of Australians. It can be life-threatening, result in lost school or work attendance and be intensely unpleasant for the patient.

Allergy assessment in routine clinical practice

All secondary immune responses result from previous exposure, including allergy, although that exposure may be difficult to identify (e.g. food allergens in infants or toddlers). The exposure history is usually centred on the clinical manifestation of allergic or possible allergic symptoms and signs. These may be obvious, particularly with food allergy where oral symptoms may arise within seconds to minutes following exposure (oral allergy syndrome, OAS), or they may require more or less detailed examination of the environment.

Some simple approaches may be useful in persons with limited allergies: pollens are prominent outdoors in spring and summer; house dust mite indoors and year-round; animal dander following specific exposures.

There are also many overlapping allergies due to the fact that allergens are often highly conserved, shared peptides in related species (e.g. certain foods, pollens, insects). This information is important in selecting laboratory testing for specific IgE, which can be used to manage severe or nuisance allergies through avoidance and/or immunotherapy.

Both skin prick testing (SPT) and serum-specific IgE are useful for identifying the presence of allergen-specific IgE in a given patient and are useful in the assessment of allergic rhinitis. However, the presence of antibody does not equal disease, and results must be interpreted in the clinical context.

Common respiratory allergens

- House dust mite
- Pollen
- Animal dander
- Mould

Food allergens present several diagnostic difficulties, partly because only certain foods or components are mandated in labelling by Australian food standards, and partly because of unseen contamination (e.g. during food preparation). Furthermore, some non-food items (e.g. cosmetics) may contain food allergens. Food ingestion may result in a variety of clinical manifestations, ranging from OAS and skin reactions to life-threatening anaphylaxis. Most food allergens are primarily managed by avoidance, but diets can be restrictive, so it is important to correctly identify the relevant allergen.

According to current information, ASCIA states that food allergy occurs in around 2-4% of Australian and NZ adults, with increased numbers in childhood (5-10%) and up to about 10% in infants. Again, SPT and specific IgE are useful for identifying the presence of allergen-specific IgE in a given patient. Elimination diets and challenge may be required but should be conducted under specialist advice and supervision.

Common food allergens

- Egg
- Cow's milk
- Peanut
- Tree nuts (most commonly cashew, pistachio, hazelnut and walnut)
- Sesame
- Soy
- Fish
- Shellfish
- Wheat

Adverse drug reactions (ADRs) are probably the most complex clinical events requiring consideration of an allergic response. ADRs are classified Type A if they are predictable due to the known properties of the drug and Type B if they are unpredictable or idiosyncratic. Type B reactions include allergic reactions that may be IgE-mediated immediate responses (including anaphylaxis) or several cell-mediated immune responses.

The clinical history is crucial in assessing drug reactions of all types. While serum-specific IgE is available for the investigation of some potential drug allergies, specialist clinical assessment some be required. It is important to consider de-labelling some patients who believe they are penicillin-allergic, since potentially important therapeutic interventions may be unnecessarily curtailed.

Insect venoms are an important cause of allergy, including anaphylaxis. Specific IgE is available for most clinically important insect venoms.

For further information about allergy testing at Clinical Labs, including our doctor brochure, allergen-specific IgE order form, clinical articles and current pricing, please visit clinicallabs.com.au/doctor/allergy.

How to Order Allergen-Specific IgE Testing at Clinical Labs

What to write on the request form:
Complete a Clinical Labs General Pathology Request Form, specifying serum-specific IgE testing. To indicate the specific allergens or mixes required, use the Allergen-Specific IgE Order Form, available at clinicallabs.com.au/doctor/allergy.

Please be as specific as possible in your selections, based on the patient's detailed clinical history.

Please note:

- Allergen mixes are best used to refine the direction of individual allergen requests, which have better sensitivity and specificity prior to treatment.
- In children, due to lack of sensitivity and specificity, and to prevent unnecessary food avoidance, testing for individual allergens is preferred over mixes.
- When one penicillin allergen is ordered for sensitivity testing, such as Amoxycillin, Clinical Labs will routinely test all four available penicillins individually as standard practice.

Test cost and Medicare eligibility:
Medicare will fund up to four patient episodes of Allergen-Specific IgE testing within any 12-month period. Each episode may include four single allergens, four allergen mixes or any combination of four allergens and mixes. If tests are not ordered together, each additional episode will require a new referral and specimen collection.

Pricing information was accurate at the time of publication. For the most up-to-date pricing, please visit clinicallabs.com.au/doctor/allergy.

> *Exposure history may be obvious or may require a more detailed examination of the environment. This information is important for selecting laboratory testing for specific IgE.*

References and further reading

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- Australian Society of Clinical Immunology and Allergy www.allergy.org.au

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Trichomonas vaginalis:
The overlooked STI

By Dr Sudha Pottumarthy-Boddu

Trichomoniasis is the most common curable, non-viral sexually transmitted infection (STI) worldwide. It is caused by the single-celled protozoan parasite *Trichomonas vaginalis* (TV). In 2020, the World Health Organization (WHO) estimated 156 million new cases globally among individuals aged 15 to 49 years.

Despite its prevalence, the true incidence remains unknown, as trichomoniasis is not a notifiable disease, except in the Northern Territory, and screening criteria are undefined. It has also been referred to as "the neglected STI" due to limited knowledge of its sequelae and associated costs.

Symptoms of trichomoniasis

- 70 to 80% of individuals experience minimal or no genital symptoms
- Men may present with urethritis, epididymitis or prostatitis
- Women may present with vaginal discharge, which can be profuse, malodorous or yellow-green
- In women with HIV, trichomoniasis is associated with an increased risk of pelvic inflammatory disease (PID)

Trichomonas vaginalis is associated with significant reproductive morbidity, including increased risk of preterm birth, premature rupture of membranes and small-for-gestational age infants. Infection is also associated with a 1.5-fold increased risk of HIV acquisition.

Diagnosis

Wet-mount microscopy is an inexpensive point-of-care (POC) test used to diagnose *Trichomonas vaginalis* infection. However, its sensitivity is poor (≤ 66%) and declines rapidly to 20% within one hour of sample collection. Culture, with a sensitivity of 63-75%, may be used in conjunction with wet-mount microscopy to improve performance. However, it is labour intensive and can delay diagnosis by up to 7 days.

> *NAATs provide a rapid method for accurate diagnosis of Trichomonas vaginalis, with sensitivity and specificity > 95% (95.2–100%).*

Nucleic Acid Amplification Tests (NAATs) provide a rapid and reproducible method for accurate diagnosis, with sensitivity and specificity > 95% (95.2–100%) compared to wet mount and culture. A recent study from the Melbourne Sexual Health Clinic reported a statistically significant 21% increase in *Trichomonas vaginalis* cases from 2011 to 2019, partly attributable to the shift from culture to NAAT. The diagnostic improvement with molecular methods has been widely recognised.

Treatment

- **Recommended:** Metronidazole 400 mg orally with food, 12-hourly for 7 days.
- **Alternative:** Metronidazole 2 g orally with food, single dose (less effective).
- Avoid alcohol during treatment and for 24 hours after the last dose.
- Advise no sexual contact for 7 days after starting treatment, or until symptoms have resolved and the course is completed, whichever is later.
- Recommend treatment for the current sexual partner.
- Further guidance available at sti.guidelines.org.au.

Test of cure

Not recommended unless symptoms persist.

How to Order Testing for *Trichomonas vaginalis* (TV) with Clinical Labs

What to Request:
T. vaginalis PCR or Trichomonas PCR

Specimens Required:

- A high vaginal or endocervical swab
- First-pass urine

Specimen Type:

- **A dedicated red-top dry swab or Aptima Unisex Swab kit.**
- If routine vaginal bacterial culture is also required (MC&S), please provide a blue-top gel swab as well.

Test Cost: Bulk-billed, subject to Medicare eligibility criteria.

Please scan QR code to view our current swab guide.

References

Trichomoniasis - STI treatment guidelines (2022). Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/std/treatment-guidelines/trichomoniasis.htm (Accessed: 04 June 2025).

Trichomoniasis. World Health Organization. Available at: https://www.who.int/news-room/fact-sheets/detail/trichomoniasis (Accessed: 04 June 2025).

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Australian STI Management Guidelines. Available at: https://sti.guidelines.org.au/ (Accessed: 01 October 2025).

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High-Risk Result Notifications via SMS

We're enhancing how we notify you about high-risk results, ensuring you receive urgent findings instantly via SMS so you can act without delay.

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- HGSA/RANZCOG guidelines do not recommend routine population-based screening for genome-wide chromosome abnormalities due to the absence of well-performed clinical validation studies.[1]
- Reduces unnecessary invasive follow-up procedures caused by false-positive results, one of the key advantages of NIPT over conventional combined first trimester screening.

Importance of 22q11.2 Screening

- 22q11.2 deletion occurs in approximately 1 in 1,000 pregnancies.[2]
- It is the second most common cause of developmental delay and congenital heart disease after Down syndrome.[3]
- Maternal age is not a risk factor. 22q11.2 deletion can occur in any pregnancy.[3]

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References

1. Prenatal screening and diagnostic testing for fetal chromosomal and genetic conditions. https://ranzcog.edu.au/RANZCOG_SITE/media/ RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20 guidelines/Clinical-Obstetrics/Prenatal-screening_1.pdf?ext=.pdf
2. Grati *et al. Prenat Diagn*. 2015 Aug; *35*(8): 801-9.
3. Rauch *et al. Am J Med Genet A.* 2006 Oct 1; *140*(19): 2063-74.

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