

Summary

- Specialist teams led by Professor David Sanders in Sheffield and Dr Jeremy Woodward in Cambridge were approved in 2018 by the NHS, for a Rare Diseases Collaborative Network (RDCN) for non responsive and refractory coeliac disease.
- Clinicians seeing any cases of suspected refractory coeliac disease should make early contact with the RDCN to give patients access to definitive diagnostic tests and novel therapies.



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Non responsive and refractory coeliac disease

Most patients with coeliac disease achieve histological and clinical remission when following a gluten free diet. However, a minority of patients do not achieve mucosal recovery and symptoms may persist despite strict adherence to a gluten free diet.

Non responsive coeliac disease is defined as persistent symptoms, signs or laboratory abnormalities typical of coeliac disease despite strict adherence to a gluten free diet for 6-12 months.

Refractory coeliac disease (RCD) is defined as persistent or recurrent malabsorptive symptoms and signs with villous atrophy despite adhering to a strict gluten free diet for more than 12 months.

There are two types of RCD:

- **RCD1** is indistinguishable from non responsive coeliac disease. It may be due to super sensitivity to trace amounts of gluten that would not affect most people with coeliac disease.
- **RCD2** is characterised by the expansion of a population of phenotypically aberrant intraepithelial lymphocytes (IELs) which lack expression of surface CD3 and CD8 but express intracellular CD3. This phenotype is present in normal individuals, coeliac disease and RCD1, but at lower frequencies. Therefore clonality is not an adequate indicator of RCD2. Quantification of the aberrant IEL subset is necessary for diagnosis, a test available through the RDCN.



Refractory Coeliac Disease

Rare Disease Collaborative Network

The RDCN

In 2018, NHS England designated teams led by Prof David Sanders in Sheffield and Dr Jeremy Woodward in Cambridge as the two national centres in the first ever UK Rare Disease Collaborative Network (RDCN).

The RDCN for non responsive and refractory coeliac disease aims to refine diagnostic and therapeutic techniques, and to develop a national database to further the understanding of the conditions and facilitate trials of treatment.

Why contact the RDCN?

Referrals to the RDCN remain lower than the expected prevalence of RCD. Clinicians who have any cases of suspected RCD (Type 1 or 2) can contact the RDCN david.sanders1@nhs.net and jeremy.woodward@nhs.net.

The RDCN can provide clinical support at various levels, such as reviewing notes, histological review, telephone consultation (with patient and/or clinician) or by seeing the patient, undertaking small bowel biopsy and investigations such as flow cytometry.

True refractory coeliac disease is rare and is likely to be over diagnosed in people with coeliac disease because without access to specialist tests, it is difficult to differentiate between refractory

coeliac disease, non responsive coeliac disease and accidental gluten exposure, slow response to treatment and super sensitive patients. Making contact with the RDCN provides access to definitive testing for RCD2, if required.

Immunohistochemistry for T-cell markers or polymerase chain reaction (PCR) for T cell receptor clonality are unreliable diagnostic tests for RCD. Flow cytometry is available via the RDCN and provides a definitive diagnosis of RCD2 by identifying individual IELs isolated from fresh intestinal biopsies.

Management of RCD

Obtaining the correct diagnosis also has important implications for treatment. Specific treatments for RCD1 and RCD2 exist, including the use of topical steroids or azathioprine for RCD1 and cladribine and autologous stem cell transplantation for RCD2. Part of the remit of the RDCN is to refine therapeutic techniques and facilitate treatment trials.

Support for your patients

We have developed patient information which you can share with patients with non responsive or refractory coeliac disease at www.coeliac.org.uk/rcd.

More information

The RDCN has published a summary of management of adult coeliac disease which includes an algorithm for investigating patients with persisting symptoms. Access this at: <https://fg.bmj.com/content/11/3/235>.

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www.coeliac.org.uk