

BACKGROUND

Cryopyrin-Associated Periodic Syndromes (CAPS) are rare, potentially life threatening auto-inflammatory disorders. Three separate CAPS are recognised: Familial Cold-Auto-Inflammatory Syndrome (FCAS), Muckle Wells Syndrome (MWS) and Neonatal Onset Multi-Inflammatory Disorder (NOMID)¹. The conditions represent a continuum of disease, with FCAS being the mildest and NOMID being the most severe^{1, 2}. The disorders are associated with mutations of the NLRP3 gene (also known as CIAS1)¹. However a mutation may be only found in up to 60% of patients, suggesting genetic heterogeneity².

NOMID is characterised by systemic inflammation with onset in infancy, and skin, joint and central nervous system all being susceptible². Delays in diagnosis result in significant morbidity, including destructive arthritis, aseptic meningitis, deafness and neurological delay². Inflammation in MWS is periodic, and although deafness is common, neurological inflammation is not². Skin and joint inflammation in FCAS is sporadic and typically occurs when the patient is exposed to cold temperatures².

Delays in diagnosis are often reported in those with CAPS. Some individuals are not diagnosed until late childhood or adult life, despite neonatal or infantile onset features of systemic inflammation^{3, 4}. Treatment with anti-IL-1 receptor antagonist therapy has revolutionised the management of CAPS, inducing rapid symptom resolution, stabilisation of white matter loss, and in some cases reversal of hearing loss⁵⁻⁷. Early recognition and treatment of CAPS is therefore of paramount importance to prevent permanent joint, hearing and brain injury.

STUDY OBJECTIVES

This study gives a unique opportunity to determine the number of Australian children with CAPS and to determine:

- Estimated prevalence of CAPS
- Time delay to diagnosis
- Presenting clinical features
- Profile of the genetic mutations detected
- Complications and outcomes associated with CAPS
- Therapy currently used

REPORTING INSTRUCTIONS

You will receive a **special one-off CAPS report card**. This CAPS report card is separate to the usual APSU report card and will be sent only once. Please indicate whether you currently have a child with CAPS under your care and return the card to APSU.

If you indicate that you have a child with or whom you suspect may have CAPS, a separate CAPS questionnaire will be sent to you via email or post, or may be downloaded from the APSU website (www.apsu.org.au). Once completed, please return the questionnaire by fax or post as instructed on the questionnaire.

CASE DEFINITION

1. CIAS1/NLRP3 mutation positive OR

2. At least one cutaneous feature

- Chronic (≥ 6 weeks) urticarial like rash developing within first 12 months of life
- Urticarial like rash only precipitated when exposed to cold temperatures.

AND at least one neurologic, rheumatologic or treatment criteria fulfilled

At least 1 Neurological feature

- Chronic headache (i.e. at least 15 headaches/month for ≥ 3 months)
- Aseptic meningitis on lumbar puncture
- Macrocephaly (head circumference $> 95\%$ percentile)
- Developmental delay
- Sensorineural deafness
- Papilledema
- Hydrocephalus
- Cerebral atrophy on brain MRI or CT

AND/OR at least 1 Rheumatologic manifestation

- Arthropathy induced by exposure to cold temperatures
- Arthritis
- Deforming arthropathy on plain X-ray

AND/OR treatment response

- There is a positive response to anti-IL-1 receptor antagonist therapy (Anakinra, Rilonacept or Canakinumab).

INVESTIGATOR CONTACT DETAILS (*Principal Investigator and contact person)

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This project has been approved by The Children's Hospital at Westmead Ethics Committee. If you have any concerns about the conduct of this study, please do not hesitate to contact the Research Ethics Manager, Secretary of the Ethics Committee (02 9845 3017) and quote approval number 10/CHW/64.