

# PRIMARY ADRENAL INSUFFICIENCY IN YOUNG BOYS IS A RED FLAG FOR ALD

- Adrenoleukodystrophy (ALD) is a frequent cause of primary adrenal insufficiency in young boys who present in the absence of adrenal antibodies<sup>1</sup>
- ALD is a rare X-linked disorder resulting from mutations in the *ABCD1* gene.<sup>2</sup> The early symptoms of ALD are similar to other medical conditions, making diagnosis challenging<sup>3</sup>
- ALD may develop into cerebral ALD, a severe form of the disease<sup>2</sup>
- Cerebral ALD leads to severe neurodegeneration and often death within a decade of diagnosis<sup>1,4,5</sup>

## SOME FACTS ABOUT ALD

- Roughly 80% of young boys diagnosed with ALD also had some form of adrenal insufficiency<sup>6</sup>
- ALD occurs in about 1 in 21,000 males<sup>7</sup>
- Causes impaired peroxisomal  $\beta$ -oxidation of very long chain fatty acids (VLCFA), resulting in accumulation of VLCFA in plasma and tissues<sup>8</sup>
- Clinical manifestation of ALD varies widely, even among members of the same family.<sup>7</sup> Patients may exhibit a variety of phenotypes, such as adrenal insufficiency, adrenomyeloneuropathy (AMN) affecting the spinal cord and peripheral nervous system in adults, or the rapidly progressive cerebral form (cerebral ALD).<sup>8</sup>
- Early symptoms are variable and non-specific but may include behavioral or learning issues and audiovisual impairment<sup>4,8</sup>
- About 35-40% of boys with ALD will develop cerebral ALD which leads to progressive behavioral, cognitive, and neurologic deficits and, in most patients, total disability and death within a decade of diagnosis<sup>4,5</sup>
- Symptoms of cerebral ALD generally present between the ages of 3 to 12<sup>1,5</sup>

## MEASUREMENT OF VLCFA LEVELS IN PLASMA MAY HELP DIAGNOSE ALD

- Increased plasma levels of VLCFA are suggestive of ALD<sup>4</sup>
- Boys with primary adrenal insufficiency who are negative for 21-hydroxylase antibodies should be assessed for ALD by measuring VLCFA levels in plasma<sup>9</sup>
- If you suspect ALD, refer the patient to a pediatric neurologist<sup>3</sup>

## EARLY DIAGNOSIS OF ALD COULD SAVE A LIFE

- Cerebral ALD can be treated with hematopoietic stem cell transplantation if the disease is diagnosed in its early stages<sup>2,3</sup>
- Early diagnosis gives boys with cerebral ALD the best chance at positive long-term outcomes<sup>3,10</sup>



## WHEN YOU SEE ANTIBODY-NEGATIVE PRIMARY ADRENAL INSUFFICIENCY—CHECK FOR ALD

**References:** 1. Engelen M, Kemp S, de Visser M, et al. X-linked adrenoleukodystrophy (X-ALD): clinical presentation and guidelines for diagnosis, follow-up and management. *Orphanet J Rare Dis.* 2012;7:51. 2. Miller WP, Rothman SM, Nascene D, et al. Outcomes after allogeneic hematopoietic cell transplantation for childhood cerebral adrenoleukodystrophy: the largest single-institution cohort report. *Blood.* 2011;118(7):1971-1978. 3. Moser HW, Mahmood A, Raymond GV. X-linked adrenoleukodystrophy. *Nat Clin Pract Neurol.* 2007;3(3):140-151. 4. Engelen M, Kemp S, Poll-The BT. X-linked adrenoleukodystrophy: pathogenesis and treatment. *Curr Neurol Neurosci Rep.* 2014;14(10):486. 5. Mahmood A, Dubey P, Moser HW, Moser A. X-linked adrenoleukodystrophy: therapeutic approaches to distinct phenotypes. *Pediatr Transplant.* 2005;9 (suppl 7):55-62. 6. Dubey P, Raymond GV, Moser AB, Kharkar S, Bezman L, Moser HW. Adrenal insufficiency in asymptomatic adrenoleukodystrophy patients identified by very long-chain fatty acid screening. *J Pediatr.* 2005;146(4):528-532. 7. Bezman L, Moser AB, Raymond GV, et al. Adrenoleukodystrophy: incidence, new mutation rate, and results of extended family screening. *Ann Neurol.* 2001;49(4):512-517. 8. Kemp S, Huffnagel IC, Linthorst GE, Wanders RJ, Engelen M. Adrenoleukodystrophy – neuroendocrine pathogenesis and redefinition of natural history. *Nat Rev Endocrinol.* 2016;12(10):606-615. 9. Bornstein SR, Allolio B, Arlt W, et al. Diagnosis and treatment of primary adrenal insufficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2016;101(2):364-389. 10. Raymond GV, Aubourg P, Paker A, et al. Survival and functional outcomes in boys with cerebral adrenoleukodystrophy with and without hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant.* 2019;25(3):538-548.