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Addison's patients lack killer immune cells: study

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Research led by University of Birmingham scientists has found that people suffering from the adrenal disorder known as Addison's disease suffer from an immune system defect which makes them prone to potentially deadly respiratory infections.

The study, published online in the *European Journal of Endocrinology*, shows for the first time that patients with primary adrenal insufficiency (PAI) have natural killer immune cells (NK) – providing frontline protection against invading pathogens – which are not functioning properly.

It concludes that this might explain why Addison's patients are prone to respiratory infections which have been shown previously to contribute to an increased risk of premature death in affected patients.

Patients with adrenal insufficiency have also been reported to suffer from an increased rate of non-fatal infections, with a 1.5-fold increased risk of use of anti-microbial agents and a 4.0- to 5.0-fold increased risk of hospital admission for infection, with rates of pneumonia reported to be more than nine times higher in adrenal insufficiency patients. However, despite well-documented reports about increased incidence and severity of infection among PAI patients, it was not known why they succumb more readily to infections than the general population.

Daily corticosteroid replacement therapy is the standard treatment for adrenal failure, and since its introduction, life expectancy of PAI

patients has increased considerably. But despite ready availability of corticosteroid replacement, Addison's patients not only suffer from a poorer quality of life but from an increased risk of premature death.

This was a collaborative study carried out by researchers from the Institute of Metabolism and Systems Research and the Institute of Inflammation and Ageing at the University of Birmingham. They analysed the function and surface phenotype of the white blood cells known as neutrophils and NK cells in a cohort of patients with PAI receiving chronic corticosteroid replacement in comparison to sex- and age-matched healthy controls to discover whether defects in innate immunity might explain the increased susceptibility to infection.

Study lead Professor Wiebke Arlt comments: 'We found that NK cells isolated from patients with PAI are not able to kill invading cells as efficiently as they should. As NK cells are involved in the early recognition and elimination of virus-infected cells, this defect may be an important factor underlying the increased incidence and severity of viral infections reported by PAI patients.'

The immune system, including NK cells, is programmed by clock genes that react to the differences in corticosteroid secretion by the adrenal gland that occur during the day. Patients with adrenal insufficiency take cortisol replacement therapy that cannot mimic this diurnal pattern, which might explain the defect in NK cells that was observed.

Professor Arlt explains "We will now examine this in more detail and try to find out whether novel cortisol replacement tools that mimic the diurnal rhythm of hormone secretion could restore NK cell function in Addison's patients back to normal."

More information: Irina Bancos et al. Primary adrenal insufficiency is associated with impaired natural killer cell function: a potential link to

increased mortality, *European Journal of Endocrinology* (2017). DOI: 10.1530/EJE-16-0969