Copper toxicosis is a genetic disease of Bedlington Terriers in which **copper accumulates** within the **liver** due to a metabolic failure to excrete it in the bile. This leads to **acute hepatic necrosis** and for those dogs surviving this **chronic hepatitis** and **cirrhosis**. In the acute phase or form of the disease there is **haemolytic anaemia**, adding pre-hepatic jaundice to any existing hepatic jaundice. There is an accompanying **regenerative erythroid response**; hence the possible relevance to these haematology results. The exact mechanism of haemolysis is unknown but thought to be related to a sudden release of copper from the liver into the circulation.

Inheritance of the disease is by at least one **autosomal recessive gene** with dogs that are clear or carriers or affected. A mutation of the COMMD1 gene has been identified as one cause of copper toxicosis in Bedlington Terriers. Initially only identifiable indirectly by a marker test, since 2005 it has been possible to screen for this mutation by a DNA test.

All dogs detailed in this poster have been tested Negative for this gene.

However there has been speculation that another gene or other genes may also be involved or capable of causing copper toxicosis in the breed.

Red blood cells are produced in the bone marrow under the control of erythropoietin, secreted by the kidneys. This secretion is in response to **renal tissue hypoxia**. **Reticulocytes** are created in the penultimate step of red cell maturation. They are released from the bone marrow after 24-48hrs and mature in the blood stream over a further 24-48hrs; losing their endoplasmic reticulum and becoming red blood cells. **Renal hypoxia** can occur due to **anaemia** and therefore a lack of oxygen-carrying capacity within the blood or due to **pulmonary factors** leading to reduced oxygenation of the red blood cells e.g. lung disease or high altitude. In these situations immature red blood cells, particularly reticulocytes are released earlier in their development and in greater numbers than usual in order to increase the oxygen-carrying capacity of the blood. This is the **regenerative response**.

Asymptomatic Reticulocytosis in a Family of Bedlington Terriers

MUPPEY
Female (neutered), born Nov. 2005.

Grandmother to Liffey but unrelated to Izzy.

16/05/2018 blood test due to pica (eating compost)
RBC = $7.86 \times 10^{12}/L$
Absolute Reticulocyte Count = $187 \times 10^9/L$

29/05/2018 x-ray chest, scan liver, spleen & kidneys
NAD
bile acid stimulation test = Not significantly abnormal
RBC = $6.99 \times 10^{12}/L$
Absolute Reticulocyte Count = $158 \times 10^9/L$

07/06/2018 further blood test to check for resolution
RBC = $8.27 \times 10^{12}/L$
Absolute Reticulocyte Count = $172 \times 10^9/L$

04/03/2019 poor appetite, blood test, no specific diagnosis
RBC = $8.38 \times 10^{12}/L$
Absolute Reticulocyte count = $211 \times 10^9/L$

22/11/2019 upper resp. tract noise, no specific diagnosis
RBC = $7.86 \times 10^{12}/L$
Absolute Reticulocyte Count = $154 \times 10^9/L$

23/12/2019 bilious and retching, pancreatitis diagnosed
RBC = $7.96 \times 10^{12}/L$
Absolute Reticulocyte Count = $153 \times 10^9/L$

IZZY
Female (neutered), born Feb. 2010

Mother of Liffey, but unrelated to Muppey

15/06/2018 routine pre-dental blood test
RBC = $8.07 \times 10^{12}/L$
Absolute Reticulocyte Count = $145 \times 10^9/L$
In the light of prior knowledge of another senior Bedlington terrier, unrelated but in the same household, with asymptomatic reticulocytosis and in the absence of any clinical illness or other significant findings no further investigation was undertaken.

11/02/2020 blood test to investigate polydipsia
RBC = $7.26 \times 10^{12}/L$
Absolute Reticulocyte Count = $115 \times 10^9/L$

19/02/2020 blood test to assess clinical anaemia
RBC = $2.38 \times 10^{12}/L$
Absolute Reticulocyte Count = $95 \times 10^9/L$

20/02/2020 Izzy was put to sleep due to an invasive adrenal tumour and gastro-intestinal bleeding

LIFFEY
Female (neutered), born April 2012.

Granddaughter of Muppey and daughter of Izzy

20/07/2018 routine pre-dental blood test.
RBC = $8.04 \times 10^{12}/L$
Absolute Reticulocyte Count = $171 \times 10^9/L$
Given the knowledge of reticulocytosis in grandmother and mother with no clinical illness or other significant findings no further investigation was undertaken.

Footnote
This poster was prepared for BSAVA 2020. While in preparation a fourth Bedlington Terrier in the same household was shown to have asymptomatic reticulocytosis.

GERTIE
Female (neutered), born April 2016.

No relation to any of the other 3 dogs.

12/02/2020 blood test as part of routine health check.
RBC = $7.29 \times 10^{12}/L$
Absolute Reticulocyte Count = $156 \times 10^9/L$
Again in the absence of any clinical symptoms no further investigation was undertaken.

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NORMAL RANGES and CLASSIFICATIONS
Red Blood Cell count $5.00 - 8.50 \times 10^{12}/L$
Absolute Reticulocyte count $< 100 \times 10^9/L$ Non-regenerative
Absolute Retic. count $100 - 175 \times 10^9/L$ Mild regeneration
Absolute Retic. count $175 - 300 \times 10^9/L$ Moderate regen.
Absolute Retic. count $> 300 \times 10^9/L$ Marked regeneration