

Anaemia in old and very old age: to be or not to be, that is not the question anymore

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Anaemia is common in older persons, especially in very old patients who often experience multimorbidity and may be institutionalised. Senescence, the ageing process, puts older persons at risk of developing anaemia for multiple reasons, but anaemia may not be attributed to senescence unless a thorough diagnostic workup has excluded other aetiologies. In 1994 the World Health Organisation (WHO) put an end to all suggestions that anaemia goes with old age and that reference values should be adapted for this group. Anaemia should therefore not be accepted as an inevitable consequence of ageing. A cause is found in approximately 80% of all old and very old patients. The most common causes of anaemia in the elderly patient are chronic disease and iron deficiency. Vitamin B12 deficiency, folate deficiency, gastrointestinal bleeding and myelodysplastic syndrome are among other causes of anaemia in old and very old age.

The most commonly used screening methods for the presence of anaemia in a person are the measurements of haemoglobin or haematocrit concentration (WHO 1994). These measurements are relatively simple and cheap, can be carried out under field conditions, and values below a certain cut-off point indicate or define that anaemia is likely to exist. The cut-off value defining anaemia has been determined by convention as the value at -2 SD from the mean or the 2.5th percentile of the normal distribution of a healthy population.

Even though the high prevalence of anaemia in older persons makes it a condition that physicians expect to find frequently, several features of anaemia make it easy to overlook. The onset of symptoms is often more or less insidious, and many old and very old patients adjust their activities as their bodies make physiological adaptations for their current condition. Typical symptoms of anaemia, such as an increased heart rate, fatigue, weakness and dyspnoea, are non-specific in older patients and tend to be attributed to an advancing age. In their review, Den Elzen

et al. describe many aetiologies of anaemia in old and very old persons and thoroughly summarise the literature on a number of diagnostic and therapeutic algorithms, especially for older patients.¹ These are important as, also in old age, anaemia is associated with functional and cognitive decline, institutionalisation and mortality. But they also remark that most studies on anaemia have been performed in patients in hospital wards and residents in institutions for older persons and not in very old persons from the general population. They state furthermore that data have become available that question the extrapolation of 'common' medical knowledge to the highest age groups in this population.

Den Elzen asks for attention for normal and subnormal vitamin B12 serum levels. These situations are sometimes also associated with pernicious anaemia but do not necessarily need the same treatment regime, lifelong intramuscular vitamin B12 supplements.

Treatment of pernicious anaemia has a peculiar history: The treatment for vitamin B12 deficient anaemia was first devised by Murphy who bled dogs to make them anaemic and then fed them various substances to see what (if anything) would make these dogs healthy again. He discovered that the ingestion of large amounts of (raw) liver seemed to cure the disease. Minot and Whipple then set about chemically isolating the curative substance and ultimately were able to isolate vitamin B12 from the liver. All three shared the 1934 Nobel Prize in Medicine.

Another interesting topic brought about is hepcidin, a main regulator of iron homeostasis, which was shown to play an important role in the anaemia of (chronic) inflammation. Only recently serum hepcidin assays have become available. Besides iron, they reviewed the roles of erythropoietin, the role of telomere length in anaemia with an unknown cause, myelodysplastic syndromes or other types of bone marrow failure, and C-reactive protein and other potential biomarkers in diagnostic algorithms of anaemia in old and very old persons.

Meanwhile, geriatricians, internists and other physicians have to deal with a large number of patients with significant anaemia but also with an absence of well-constructed standards and guidelines for the old and very old patient with and without multimorbidity. The article by Den Elzen *et al.* should raise awareness that anaemia in these groups is multifactorial and that these patients are more than merely older than those included in most studies, that the results of ongoing and even future trials should be appropriately interpreted and will be important in guiding practice in the next two or three decades.

REFERENCE

1. Den Elzen WPJ, Gussekloo J. Anaemia in older persons. *Neth J Med.* 2011;69:260-7.