Commentary

Hyperimmune goat serum (Aimspro®): Hope or hype?

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In March 2005, newspaper and television reports from the UK suggested that treatment with Aimspro®, a 'hyperimmune goat serum' (HGS), resulted in an improvement in symptoms attributed to multiple sclerosis. In September 2005, the Hansard record of UK parliamentary debates noted while at least 250 people with multiple sclerosis had received this product, it was unlicensed and a report by the UK Medicines and Healthcare Regulatory Agency (MHRA), had found 'critical and major deficiencies concerning good manufacturing practice'. Furthermore, the MHRA had previously requested that product manufacturers, Daval International Ltd, remove misleading claims regarding HGS from its website: to date there is no data regarding mechanism of action or demonstration of clinical efficacy in a placebo-controlled trial that has been published in a peer-reviewed full-length journal article.

Despite concerns regarding the absence of evidence for therapeutic benefit, HGS continues to be administered to patients and anecdotal treatment effects are being reported in a growing list of neurological disorders that includes myasthenia gravis, Krabbe's disease, CIDP, Charcot-Marie-Tooth, and fascioscapulohumeral dystrophy. These case studies have either been reported as abstracts documenting meeting proceedings or referred to in a previous open label study that was published in this journal (epublished ahead of print 13 March 2006; withdrawn by authors 4 April 2006).[1] In this issue, the effects of HGS administration are described in an individual with motor neuron disease demonstrating increasingly widespread use of this product.[2] In view of the lack of published data, we have attempted to review available information in order to provide neurologists with an overview on the current status of HGS.

Since HGS is derived from animals immunized with inactivated HIV virus, it seems something of a 'knight's move' that a strategy intended to produce neutralizing antibodies for the treatment of HIV should be mooted as a therapy in neurological disorders of such diverse aetiology. At present there is no published data regarding a definitive mechanism of action of HGS; however, it is suggested by the authors that the serum of immunized goats contains high titres of antibodies that react with the human HLA class II antigens and that these anti-HLA antibodies account for 'anti-inflammatory properties' attributed to this product.[2] Studies on purified HIV preparations have demonstrated that specific cellular antigens, including HLA class II antigens, are incorporated into the surface of the virus and selective incorporation of between 375 and 600 HLA DR (α and β chains) molecules per virion means that this protein actually outnumbers the 216 molecules of the virus envelope glycoprotein gp120.[3] The immunogenicity of these incorporated class II DR antigens is confirmed by the observation that there is significant induction of anti-class II antibodies (in the absence of allostimulation) in haemophiliacs after HIV infection.[4] Therefore, an 'unpublished observation that HGS inhibits a variety of mixed lymphocyte reactions'[1] is consistent with the hypothesis that HGS contains antibodies reacting with HLA class II DR, which can interfere with antigen presentation.

Although the pathogenesis of MS remains poorly defined, there is a significant inflammatory component to the disease[5] and a robust and reproducible observation is that the HLA class II allele DRB1*1501 is the single most important susceptibility gene, in Caucasians,[6] with other class II alleles being more relevant in non-Caucasian races. Thus there is a rationale for HGS to be considered as a potentially immunomodulatory therapy in MS. Nevertheless, while the results of an uncontrolled and unblinded open label study into the use of HGS in six multiple sclerosis patients with chronic optic neuropathy failed to meet the primary endpoints of improved visual acuity or improvement in VEP latencies, great emphasis was placed on rapid restoration of a single previously unobtainable visual evoked potential and an apparent improvement in colour vision within 1 hour following administration of HGS.[1] It is evident that these clinically unhelpful, apparent responses, cannot be attributed to an immunomodulatory effect in patients with stable visual dysfunction due to chronic optic neuropathy of 8–16 years duration. Therefore the authors interpreted these findings to be due to reversal of axonal conduction block,[1] which in turn is implied to have been present for years without accompanying axonal degeneration. The discussion does not suggest any biologically feasible mechanism to explain the incongruous observation of an improvement in colour vision or VEP in the absence of an improvement of visual acuity, other than acknowledging that the observed results of colour vision testing may be

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consistent with the well known fact that the Farnsworth-Munsel Hundred Hue Test is subject to learning effects.

The only placebo-controlled trial of this product that we are aware of which has been completed to date is the Oxford Optic Neuritis Trial.[7] While the complete dataset from this study remains unpublished, it has been reported that treatment with HGS demonstrated no improvement in the primary or secondary outcome measures of visual evoked potential amplitude or latency and the fMRI BOLD response. Furthermore, a statistically significant improvement in a visual field tertiary outcome measure ($p < 0.05$), turned out to be a specious result when compared to the effects obtained with placebo administration.[7]

While the unmet therapeutic demand in the treatment of MS, MND and other progressive neurological conditions remains a source of enormous frustration to those directly and indirectly affected, it is imperative that undue emphasis is not placed on selective reporting of anecdotal cases. Although Mackenzie et al.[2] document a less marked decline in respiratory muscle strength than might be expected, it is inappropriate to use a cohort of affected patients from the literature as a comparator for results obtained in one individual. In addition, there is no reason why respiratory muscle strength should be relatively preserved while that of other voluntary muscles continue to deteriorate.[2] In the absence of publications that have been subjected to rigorous peer review demonstrating biologically plausible effects of this product and clinical data from appropriately controlled studies, claims regarding the efficacy of this product in the treatment of neurological diseases must be regarded with extreme scepticism.

References

1. Youl BD, White SD, Cadogan M, et al. Goat serum product "Aimspro" restores conduction in demyelinated human optic nerve fibres. *J Clin Neurosci* 2006;**13**., epub ahead of print 13 March 2006; withdrawn by authors 4 April 2006.
2. Mackenzie R, Kiernan M, McKenzie D, et al. Hyperimmune goat serum for amyotrophic lateral sclerosis. *J Clin Neurosci* 2006;**13**.
3. Arthur LO, Bess Jr JW, Sowder 2nd RC, et al. Cellular proteins bound to immunodeficiency viruses: implications for pathogenesis and vaccines. *Science* 1992;**258**:1935–8.
4. Riera NE, Galassi N, de la Barrera S, et al. Anti-leukocyte antibodies as a consequence of HIV infection in HIV+ individuals. *Immunol Lett* 1992;**33**:99–104.
5. Barnett MH, Sutton I. The pathology of multiple sclerosis: a paradigm shift. *Curr Opin Neurol* 2006;**19**:242–7.
6. Yaouanq J, Semana G, Eichenbaum S, et al. Evidence for linkage disequilibrium between HLA-DRB1 gene and multiple sclerosis. *The French Research Group on Genetic Susceptibility to MS. Science* 1997;**276**:664–5.
7. Burke G, Matthews PM, Palace JA. The evaluation of a novel "goat serum" therapy (Aimspro) in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2006;**17**:1326.

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Pituitary abscess

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Abstract

Pituitary abscess is a rare disease, but one with potentially high mortality and morbidity. We present a 46-year-old man with progressive visual disturbance and general malaise for 1 year. Endocrine studies revealed hypopituitarism, and magnetic resonance imaging revealed a pituitary lesion with suprasellar extension. We attempted to excise the lesion using a transsphenoidal approach, but pus in the pituitary fossa was found at operation, and no tumour was identified. The culture yielded coagulase-negative *Staphylococcus*. Antibiotics were administered for 3 weeks, and the patient made a good postoperative recovery. He required life-long hormone replacement therapy. After one and a half years of follow-up, he was well and had no evidence of focal or systemic infection. We review the literature regarding pituitary abscess and discuss the appropriate treatment and possible pathological mechanism.

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