BSS 2015 Conference and AGM

The 2015 BSS Conference and Annual General Meeting took place at Friend's House, 271 Euston Road, London, on 17 October.

AGM business

Alan Booth opened proceedings and welcomed everybody. Judi Scott confirmed that the annual subscription will stay at £20 for 2015/16 and the Grant Aid limit will remain £750.

Treasurer's report

Alan Lane reported that membership of the Society is increasing. As of 1 September 2015, there were 1016 members. These included 861 full members, eight junior members and 48 associate members (mostly medical professionals). The youngest member is 12, and the oldest are in their 80s. The total also includes possibly lapsed members who will have to be deleted from the database to comply with data protection legislation if their subscriptions are not received. Most (815) members live in England, with 75 in Wales, 53 in Scotland, 26 in Northern Ireland, seven in the Channel Islands and 14 overseas.

About half (51%) of the Society's income is from donations, with 19% coming from fundraising and 18% from subscriptions. In the last year, about 25% of the money spent went on fundraising and another 25% on research grants. The spending on fundraising was higher than usual, partly due to costs associated with the London to Paris bike ride. A further 19% was spent on administration, with 13% on the newsletter and 6% on the AGM. In addition, a small proportion (3.2%) went on charitable support, such as a mobility scooter for one disabled member.

The Society's income in 2014/15 was £63,400 (compared with £73,400 in 2013/14), and expenditure was £43,300 (compared with £52,200 in 2103/14). The Society now has an operating surplus of £74,900, which is very healthy. The Society will be looking for ways to provide more services for members, as the aim is not to keep a large amount of money in the bank. The research fund, which contained £20,300 at the end of 2013/14, now has only

£6,500 after the donation from the Worshipful Company of Horners was allocated. The fund will now be built up again until it contains enough to fund some more important research.

Chair's report

Alan Booth entitled the first part of his presentation "Lost and found". The Medical Advisory Panel has lost Colin Barnes as Convenor, but gained Robert Moots as a replacement. The Helpline has lost Lynn Barnes, Janet Duckhouse and Mandy Cossham, but found Tony Wright; more volunteers are still needed. The administration of the Society lost Chris Phillips, but has now found Julie Collier. The Board of Trustees has also lost Aaron McPeake, John Henson and Amanda Moseley, and again more volunteers are needed. Alan thanked all the Trustees and their families, the Helpline volunteers and all those who have donated or raised funds for the Society.

There have been a couple of problems during the past year. The planned family weekend had to be cancelled at short notice, as the two young people who were going to attend were not well enough to travel. However, there are plans to hold the event next year. The website had a problem in the first part of the year and had to be suspended for a while. It is now more secure and is being reviewed with the aim of making it more responsive.

Alan announced that next year's AGM and Annual Conference will take place, along with the Behçet's Forum and a dinner-dance fundraiser, at the Plough and Harrow in Birmingham on 14–15 October. Finally, he reminded everyone to use the new official address for the Society and the behcetsdisease.org.uk email addresses.

Medical presentations

Overview of Behçet's disease

Prof Farida Fortune, Clinical Lead at the London Centre, began by saying that she is very committed to patient-driven research. For this, working with the BSS, and with patients worldwide, is crucial. She then pointed out that Hippocrates, a physician in classical Greece, described Behçet's disease (BD) very well. It is a multisystem disease, classically seen along

the “Silk Route”. However, migration of populations means that it is seen all over the world, although the clinical presentation varies geographically as well as between the sexes. BD has multiple types of pathogenesis, and each patient can be considered to have his or her own BD. The most common symptoms are oral ulcers, skin rashes, genital ulcers and ocular manifestations. Arthritis is also common in Western populations; it is usually associated with pain but not with structural damage to the joints.

There are various possible triggers of BD. Many patients have flares in spring and autumn, as well as in association with flu outbreaks. The microbiota (micro-organisms that live on or in the human body) is also important. A recent study of microbes in the mouth found particular species (such as Streptococcus sanguinis) associated with BD. It may be that such organisms cause a breach in the oral mucosa, leading to an inflammatory response that results in an ulcer. Oral ulcers are not diagnostic of BD, as they occur in 25–30% of the general population and are also common in several other diseases. However, the ulcers of BD have a characteristic pattern and appearance. The prevalence of ulcers can be decreased by good oral hygiene and dental health. BD patients have been found to have more dental caries and periodontal (gum) disease than would be expected in people with oral ulcers. Contributory factors in women include plaque, smoking, stress and filled teeth, while oral ulcers are more common in men with tooth decay, missing teeth and a poor diet. For BD patients with oral ulcers, it is important to use mouthwash to prevent scarring. Oral hygiene is as important a part of the treatment as drugs.

Genital ulcers occur in 86% of BD patients, mainly on the vulva in women and the scrotum in men. As in the mouth, the ulcers are associated with soreness and erosion, and they have a major impact on quality of life. A genital ulcer severity scale has recently been developed to measure the effect on patients; it was developed using patient-driven data.

The dermatological symptoms of BD, such as erythema nodosum, are all also seen in other diseases. Similarly, the ocular manifestations, comprising inflamed vessels, infiltrates and hypopyon, can have many other possible causes. The gastrointestinal symptoms of BD overlap with those of Crohn’s disease, but the treatment is the same whatever the underlying condition. Neurological manifestations can be severe, but are treatable. One BD patient, who had been lost to treatment for many years, presented with complete paralysis; after treatment with high-dose steroids, he was back walking within a week.

Psychological factors in living with Behçet's disease

Dr Sarah Douglas, Clinical Psychologist at the Birmingham Centre, explained that the psychological model used in Birmingham includes multidisciplinary team referral and self-referral, psychological screening and assessment, signposting/treatment, follow-up, and opportunities for group sessions and Skype therapy. Patients may present with a wide variety of difficulties, including anxiety, low mood/depression, fatigue, pain, psychosexual issues and cognitive problems. They often need help with adjusting to changes in their role, work, self-esteem, identity and relationships.

Patients can be signposted to psychoeducational resources, the Behçet's Support Co-ordinator or local specialist services. A few patients receive ongoing therapy at the Centre. Psychological interventions that may be used include cognitive behavioural therapy (CBT) and acceptance and commitment therapy (ACT). ACT uses approaches such as self-compassion and mindfulness, a technique in which attention is focused on the present moment and which is increasingly being used to treat stress and depression. Other interventions include narrative approaches, coping strategies, pain management and fatigue management.

Fatigue is a complex problem resulting from the cumulative effects of stress, pain and anxiety. It is important for patients to learn how to manage stress and to have self-compassion. People may have to realise what they need to accept at a given moment (for example, accepting that they cannot go through with their plans), understanding that acceptance is not the same as giving up. They should also make sure that they do something for themselves when they are feeling good, not just catching up on work or doing things for family.

One issue that BD patients have identified as a concern is being believed when they do not look ill. It can be difficult to explain to colleagues or friends that the fatigue they feel is not the same as normal tiredness after a late night or a busy week. BD patients often put on a brave face in an effort to be "normal", and other people do not realise how long it took them to get ready or how exhausted they are. Patients also have concerns about identity, feeling like "damaged goods" or guilty at how much their partner has to do. Anyone struggling with feelings like these would benefit from seeing the psychologist at one of the centres.

Recent advances in Behçet's disease research

The final medical presentation was by Dr Graham Wallace, Senior Lecturer in Immunity and Infection at the University of Birmingham. Before starting his planned presentation, he explained the scientific basis of fatigue in BD. The inflammatory response characteristic of BD comes at the cost of energy expenditure, and this investment of energy resources in inflammation means that other systems lose out. Fatigue is a way of stopping people putting energy into other things so that they can mount an inflammatory response to threats such as infections.

Dr Wallace said that many cells, cytokines (proteins that are secreted by certain cells of the immune system and have an effect on other cells) and processes are involved in BD, and it is still unclear how they all fit together. HLA-B51, a cell surface molecule that signals to cells of the immune system, has the strongest association with BD in genome-wide association studies. High levels of HLA-B51 positivity are seen in areas with high prevalence of BD, although the highest levels occur in Inuits, among whom no cases of BD are known. HLA-B controls cytotoxic T-cells, such as CD8-positive cells and natural killer (NK) cells. NK cells detect the decrease in HLA-B on virally-infected cells and tumour cells, and can then kill them. Each person's cells have two types of HLA molecules on their surface – one inherited from their mother and one from their father. People with HLA-B51 from both parents are at a higher risk of BD than those with HLA-B51 from one parent and a different protective form (or "allele") from the other. Research is ongoing to determine the effect of these protective alleles on cytotoxic T-cell function.

Dr Wallace then spoke about epigenetics – heritable changes in gene expression that do not involve changes to the underlying DNA sequence. Epigenetics explains why differences are seen even in identical twins. Individual genes can be switched on or off, for example by methylation of the DNA. Sometimes the change can become fixed, with a gene being constantly switched on. A range of factors, such as early life stress, environmental chemicals, drugs, ageing and diet, can affect epigenetic mechanisms. Differences in DNA methylation have been detected among genes involved in regulating the cytoskeleton (a network of fibres that helps the cell to maintain its shape) in BD patients compared with controls. The differences in methylation were seen to be reversed by treatment that led to disease

remission. Another epigenetic mechanism involves microRNA, small non-coding regulatory RNA that controls gene expression (and hence protein production) by binding to messenger RNA. Various microRNAs have been identified in BD patients in China, which together show a pattern of increased pro-inflammatory responses and decreased regulatory responses in BD.

The next topic discussed by Dr Wallace was metabolomics – the study of the unique chemical fingerprints that specific cellular processes leave behind. For example, profiling of the metabolites in vitreous fluid can distinguish between different types of uveitis. Metabolic fingerprinting of pre-treatment urine samples from patients with rheumatoid arthritis (RA) has been shown to predict which patients will respond best to anti-TNF therapy (for example, with infliximab). The Qatar National Research Foundation is funding a metabolomics study in RA and BD in the Middle East and UK.

There is also research going on to validate a novel machine-learning classification for the diagnosis of BD. The prolonged inflammatory response in BD results from failure to resolve inflammation efficiently, and many cytokines are involved in this. Single-cell flow cytometry is a method of analysing cells and cytokines – white blood cells are labelled and detected by lasers to see which cytokines predominate. Using traditional two-dimensional plots, BD and sarcoidosis could not be distinguished due to a large amount of overlap. The new supercell analysis method uses multiple single-cell measurements averaged over a group of 10–100 cells to overcome cell heterogeneity and allow clearer separation. With this method, sarcoidosis and BD can be separated using as few as five markers. The current research is looking at supercell analysis in the differentiation between BD and other inflammatory diseases in a larger cohort of patients. Almost 90 BD patients have been tested, as well as 20 healthy controls, eight sarcoidosis patients and 15 idiopathic uveitis patients. Preliminary results show promising separation between BD patients and controls and between ocular and non-ocular BD patients. Analysis is ongoing and the findings should be published early in 2016.

Finally, Dr Wallace gave a possible explanation for why BD exists. Recent studies have shown that modern humans interbred with Neanderthals, and most humans have 1–4% Neanderthal DNA in their genomes. HLA-B51 is derived from Neanderthal DNA. Tuberculosis is a major producer of nicotinamide (vitamin B3) and can cover its production when meat is scarce; when meat is plentiful, nicotinamide boosts host immunity to control

TB. HLA-B51 may have been very good for “controlling” TB and allowing humans and bacteria to coexist. This was useful for Neanderthals and was maintained in modern humans after interbreeding. Over time, other mutations (different in different geographical areas), which may be protective themselves, have combined with HLA-B51 to cause BD.

BPC update

John Mather, BPC Operations Manager, gave an update on the Centres of Excellence. The BSS first became aware of National Commissioning Funding in 2008, and following a lengthy bidding process, the centres were officially opened in 2012. The aims of the centres include early diagnosis or exclusion of BD, access to a range of specialists in one place, optimal care and effective management of the disease, and improved patient experience and clinical outcomes. The clinical model is multidisciplinary outpatient clinics with core specialists, and access on the day to other specialties as needed. The service is focused on patients’ needs, with continuous improvement driven by feedback.

The Support Co-ordinators at the three centres between them work with 918 patients and support around 65 clinics each quarter. In the last quarter, they met 200 patients, had consultations with 119 patients in clinic and had contact with 278 patients outside of clinic. The total number of activities (emails, phone calls, etc) was over 1,000. Feedback from patients about the Support Co-ordinators is very positive, and the most recent Quality of Life Survey completed in late 2014 showed that 80% of the 116 respondents were either “somewhat satisfied” or “very satisfied” with the centres.

In the discussion about the centres, it was confirmed that they cover patients of all ages – transitioning from child to adult services was a part of the bid. Patients can stay with their local consultants if they wish; it is possible to register with a centre but receive care locally. The centres hold the budget for high-cost treatments. The centres also have fast systems for referral to other specialists such as gynaecologists, without the need to go back to the GP. One topic raised was problems with GP services. The centres run training sessions, but these are mainly attended by junior hospital doctors rather than GPs. The doctors at the centres occasionally contact GPs to co-ordinate care or to reinforce important messages.

Clare Griffith, Editor