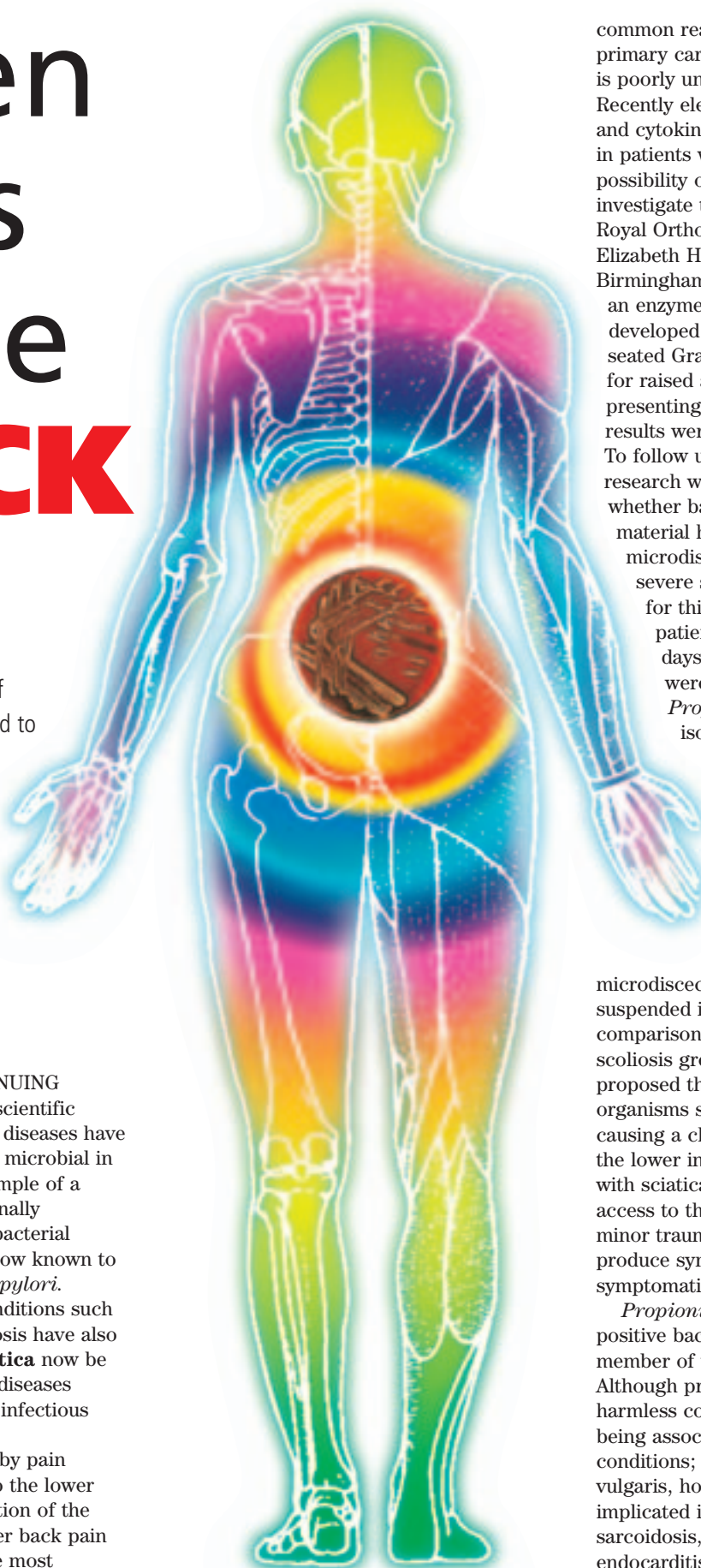


When bugs strike BACK

Alexandra Perry asks if **sciatica** can now be added to the list of diseases thought to be caused by an infectious agent?

WITH THE CONTINUING advancement of scientific techniques many diseases have been found to be microbial in origin. The best-known example of a disease which was not originally suspected to be caused by bacterial infection is gastric ulcers, now known to be caused by *Helicobacter pylori*. Infectious links to other conditions such as arthritis and atherosclerosis have also been proposed. Could **sciatica** now be added to the list of various diseases thought to be caused by an infectious agent?

Sciatica is characterized by pain radiating from the back into the lower extremities caused by irritation of the sciatic nerve. Although lower back pain and sciatica are some of the most



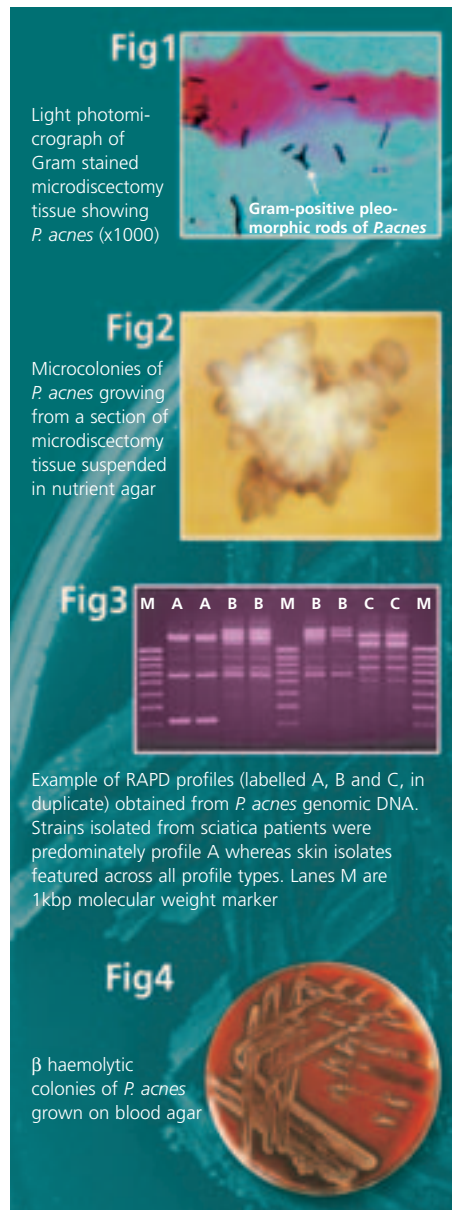
common reasons for consultation in primary care the pathogenesis of sciatica is poorly understood (Anon, 1995). Recently elevated serum immunoglobulin and cytokine levels have been described in patients with sciatica, raising the possibility of a microbial aetiology. To investigate this theory, researchers at the Royal Orthopaedic Hospital, the Queen Elizabeth Hospital and Aston University in Birmingham (Stirling *et al.*, 2001) used an enzyme linked immunoassay, developed for the diagnosis of deep-seated Gram-positive infections, to look for raised antibodies in patients presenting with severe sciatica. Positive results were observed in 31% of patients. To follow up this preliminary finding, research went forward to examine whether bacteria were present in disc material harvested during routine microdiscectomy operations to relieve severe sciatica. Control specimens for this study were obtained from patients with scoliosis. Within 7 days of incubation 53% of patients were culture positive and *Propionibacterium acnes* was isolated from 84% of the positive samples. Gram-stained smears of tissue samples embedded in agarose also showed Gram-positive branching rods after incubation (figure 1). Furthermore, *P. acnes* could be seen growing from a section of microdiscectomy tissue which had been suspended in nutrient agar (figure 2). In comparison none of the specimens from scoliosis grew bacteria. It was therefore proposed that low virulent micro-organisms such as *P. acnes* might be causing a chronic low-grade infection in the lower intervertebral discs of patients with sciatica. These organisms may gain access to the spinal disc after previous minor trauma and discs that do not produce symptoms may become symptomatic following infection. *Propionibacterium acnes* is a Gram-positive bacterium, best known as a member of the skin flora of man. Although previously thought of as a harmless commensal, it is increasingly being associated with numerous conditions; most notably with acne vulgaris, however it has also been implicated in endophthalmitis, sarcoidosis, prosthetic hip infections, endocarditis and osteomyelitis (Eady and

Ingham, 1994).

The surgical technique used in the Birmingham study used stringent aseptic techniques, however, in this and many other instances of presumed *P. acnes* infection, contamination of the samples with skin commensal bacteria always remains a possibility. This eventuality is difficult to disprove given the ubiquitous nature of *P. acnes*, but is being approached by using molecular typing techniques. Genotypic methods have been employed to determine whether infecting strains isolated from sciatica patients constitute a specific genotype in comparison to other *P. acnes* strains; in particular skin commensals. A modification of PCR called random amplification of polymorphic DNA (RAPD) which utilises short primers (8-10bp) and a series of low stringency annealing steps to amplify regions of genomic DNA has been used to type *P. acnes* strains. After multiple rounds of PCR, fragments of varying size are generated which give a specific DNA 'fingerprint' when separated by electrophoresis. Strains isolated from sciatica patients were found to be characterized by RAPD profiles distinct from profiles generated from *P. acnes* isolated from other sources (figure 3). This supports the hypothesis that an infectious strain of *P. acnes* is implicated in sciatica and that excised disc material is not becoming contaminated with skin commensal strains during surgery. Further study is currently being undertaken to genotype a wider diversity of strains including those found in acne lesions.

Propionibacterium acnes produce many exocellular enzymes including haemolysins, lipases, proteases, hyaluronidase and phospholipase C (figure 4). These factors may well contribute to virulence and disc pathology as this organism has the ability to degrade components of the extracellular matrix and destroy host cells. Indeed, studies have shown that exocellular enzyme production by *P. acnes* is optimal at low oxygen concentrations (Cove *et al.*, 1983). The low oxygen micro-environment of the intervertebral disc may therefore play a major role in the production of these enzymes.

In *P. acnes* endophthalmitis symptoms typically present months after cataract surgery. This violation of the eye could be likened to minor trauma of the intervertebral disc which may allow



microorganisms to access a site of immune privilege. Similarly, both the eye and the intervertebral disc are predominately avascular.

As stated earlier, inflammation has been implicated in sciatica but the cause of this is uncertain. Could *P. acnes* have a role? The immune response to *P. acnes* has been well-characterised in acne patients and proliferation of this organism in the pilosebaceous follicles of the skin is associated with the production of cytokines and other proinflammatory molecules (Leyden, 2001). *P. acnes* may therefore have a role in the initiation or modification of the inflammatory response associated with some disc herniations.

Research is currently underway to investigate the immune response of

sciatica patients to *P. acnes* in an attempt to identify potential markers of *P. acnes* infection and possible mediators of inflammation. An antigen that could be exploited for use in an ELISA would be particularly advantageous compared to microdissectomy and subsequent culture of disc material to confirm *P. acnes* infection.

The results of this research are particularly exciting however work is still in its early stages and a causal relationship between *P. acnes* and sciatica has not yet been established. If further research and potential clinical trials confirm an association between *P. acnes* and sciatica, early diagnosis could lead to improved treatment strategies such as intervention with appropriate antibiotics to modify subsequent progression of the disorder.

Could *P. acnes* be to sciatica what *H. pylori* is to gastric ulcers - a microorganism considered non-pathogenic found to be the causative agent of a 'non-infectious' condition? □

Alexandra Perry

Molecular Biosciences, Aston University

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Further reading:

You can read more about the possible role of *P. acnes* in the development of sciatica in the report by **Charlotte Hall** on page 39