



Guillain-Barre Syndrome: Harnessing the body's defences

INCREASED UNDERSTANDING OF THE IMMUNE SYSTEM IS OFFERING HOPE OF BETTER TREATMENT FOR DISORDERS SUCH AS THE NERVE-DAMAGING GUILLAIN-BARRE, WRITES ALISON GOODWIN.

PHOTOGRAPHER: EAMON GALLAGHER

To the layman's eye, at least, disorders of the nervous system, cancer, arthritis and hay fever don't appear to share much in common. Different parts of the body, and a huge difference in how they affect their victims, you might say.

One needs to look closer, much closer, to see that the world of immunology is

central to all of them. And it is the immunopathologist whose skills may have a major impact on future treatments.

How an uncommon peripheral nervous system disorder, Guillain-Barre syndrome (GBS), is treated today could give us some pointers for the direction of medical science in the future.

The beginnings of GBS can be innocuous enough; recovering from a recent viral or bacterial infection, the patient days or weeks later may report strange sensations including numbness of hands and feet.

Soon feelings of extreme lethargy, pain and muscle weakness may take hold and



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enormous potential to disrupt its victims' lives financially and emotionally.

Along with ventilation, pain relief and later rehabilitation, newer methods of treatment zeroing in on the immune system may lessen the duration of the illness.

One treatment is plasmapheresis, or plasma exchange, where the patient's blood is washed and the plasma containing harmful and beneficial antibodies is separated. Along with replacement fluid, the red blood cells, white blood cells and platelets are returned to the patient.

A second treatment, intravenous immunoglobulin – using purified pooled immunoglobulin, or antibodies, from blood collected from healthy donors – acts to block damaging antibodies causing the disease. Such treatments have been likened to starting a fire to destroy forest litter and deprive a major bush fire of its fuel.

Increased understanding of the immune system is equipping the medical world with a better arsenal of treatments for a host of other illnesses. This fight-fire-with-fire strategy has its roots in the earliest immunological techniques of vaccination, a concept developed just over 300 years ago when English country doctor Edward Jenner observed that dairy maids recovering from the relatively mild disease cow pox had protection against the similar but deadly disease smallpox.

Jenner realised that their bodies contained substances that could be used to help prevent illness in others. His monumental discovery was based on a combination of his application of scientific method using observation and

it becomes a monumental effort just to walk. Before they know it, patients may end up in an intensive care ward, unable to breathe unaided, robbed of speech and sometimes completely paralysed and in intense pain.

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Possibly as a result of a previous viral or bacterial infection, the body's defences,

unable to discriminate between normal body cells and those of the virus or bacteria, attack nerve cells' fatty outer coating (the myelin sheath) and occasionally axons, which conduct impulses away from such cells.

Confused messages are relayed to the brain by the damaged nerves and the patient may experience distorted sensations and muscle weakness.

Neither preventable nor contagious, GBS can be contracted by people of any age or either sex. Affecting about one in 100,000 Australians per year, it has

experimentation, and an uncommon amount of faith.

Immunological understanding of how the body can be assisted to fight, modify or switch off its own defences is at the core of new treatment and techniques.

The earliest vaccines were made from naturally occurring bacteria or viruses. Antigen vaccines, made from the proteins,

or antigens, in cancer cells can now be manufactured in large quantities in laboratories to stimulate a cancer patient's immune system to attack the cancer. Cancer cells can also be treated with radiation and then re-introduced to the patient's body to help stimulate the immune system.

Associate Professor Andrew Kornberg, director of neurology at the Royal Children's Hospital in Melbourne, says "small incremental steps" in understanding, rather than dramatic cures and the perfect medication, point the way for better treatments for GBS and other autoimmune disorders.

Lena's story

Lena Della-Franca is no wimp: she thought keeping active was the best way of recovering from a debilitating bout of diarrhoea in June 2003.

Her family, friends and a local doctor believed the strange collection of symptoms that plagued her would eventually disappear. The 55-year-old West Australian sensed a loss of strength in her hands and legs, her joints were aching and she had developed a "duck-waddle" walking style.

Her bowel control was affected, but a local doctor assumed this was part of her earlier infection. Soon Lena lacked the strength to turn on the kitchen tap and one morning her legs simply gave way.

"I thought, 'This is crazy', and started to wonder, 'Is this my time to go?'" she recalls.

Her family had to carry her to the car for the journey to Kalamunda Hospital on the outskirts of Perth.

"The doctor there couldn't put a name on it, but he said he thought I had 'a form of paralysis which was going to get a hell of a lot worse' and he was sending me to the 'big boys' in Perth," she says.

In the emergency ward at Perth's Sir Charles Gairdner Hospital, Lena was diagnosed with Guillain-Barre syndrome and given her first course of immunoglobulin. She spent most of the next two weeks having immunoglobulin therapy, paralysed from the waist down and drowsy from morphine to combat intense pain.

"I didn't allow it to get to me; I was not allowing mind games," she says,



describing her uncertainty about how or when she would recover.

Hospital staff had given her brochures about the syndrome, but she was too ill to take in much and in retrospect is glad she wasn't fully aware of its possible effects. Her neurologist, Dr Bill Carroll, gave her more confidence than anyone that she would eventually walk again, Lena says.

After two weeks in intensive care, Lena was transferred to a rehabilitation hospital and for the next 10 weeks had to relearn skills most of us take for granted: standing unaided, walking, dressing and using the toilet.

She can see humour now in her 15 to 20-minute struggle, unassisted, to wriggle out of wet bathers after hydrotherapy sessions.

One of four Guillain-Barre patients in rehabilitation at the time, Lena was

fortunate; she didn't need ventilation to help breathing and didn't lose her power of speech. She was unable to walk for eight weeks and it took her 12 months to regain enough strength to drive her car.

She remembers vividly the frustration of recuperation and felt that some hospital staff, used to dealing with spinal injury and stroke patients, understood very little about her condition and considered she'd recover faster simply by being more optimistic.

"It's not determination; it's what physical strengths you have and what you can do with them," she says.

Lena now walks unaided but has to avoid uneven surfaces and still hasn't recovered full feeling in the fingertips of her right hand. As part of her recovery and independence goal, she has plans for a trip to Europe.

“The breakthrough is related to choosing the best therapy for the particular condition,” he says. “By being able to distinguish between conditions in a more certain way, the therapies that have the best chance of benefit are used. More importantly, therapies that are either detrimental or associated with complications are not.

“In the past many of the conditions were treated by supportive measures alone. With the advent of immunotherapies, the underlying autoimmune process is targeted with clinical benefit. The immunotherapies suppress the pathogenic mechanisms, rather than treat the underlying cause or trigger. In some instances (intravenous immunoglobulin) is thought to ‘reboot’ the immune system with consequent improvement in the disorder.”

Research conducted by Dr Nobihuro Yoki from Niigata University, Japan, into ‘molecular mimicry’ has also produced encouraging results. Antibodies created to share an antigenic epitope with certain molecules in the central nervous system would appear to ‘mop up’ the unwanted antibodies causing the problem, allowing the axons to repair themselves. Infecting organisms identified include, campylobacter jejuni, mycoplasma pneumoniae, EB virus and cytomegalovirus.

Newer therapies including interferons and glatiramer acetate harness either the body’s own defences or employ substances made in laboratories as agents to modify or enhance the immune system’s ability to recognise, inhibit or destroy threatening substances.

Interferons, which belong to a chemical group known as cytokines, are a biological response modifier and, as their name suggests, they interfere with cells and can slow their growth.

The body makes interferons, but they can also be produced artificially in much larger quantities in laboratories. Interferon alpha, one of the first immunotherapies to treat cancer, has an ability to interfere with the division of cancer cells.

Glatiramer acetate is a synthetic compound made up of four amino acids found in myelin. It is thought to reduce inflammation by stimulating T cells in the immune system to change from being pro-inflammatory agents to anti-inflammatory agents.



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Monoclonal antibodies, proteins made in the laboratory from a single copy of a human antibody or cloned animal antibodies, are designed to recognise abnormal proteins.

A monoclonal antibody, rituximab, is being used in the treatment of certain nerve disorders associated with high levels of antibodies and also non-Hodgkin’s lymphoma. Given by infusion, it targets the B cells that produce antibodies and is used in patients not responding to other therapies.

Another monoclonal antibody is ADEPT, used in treatment of colon cancer,

and another, trastuzumab (better known by its trade name, Herceptin) targets cancer cells producing the protein HER2 in breast cancer.

From breakthroughs using medications such as rituximab, which may benefit a relatively small group of individuals, new medications are in the pipeline that hopefully will have a wider impact. 🔥

The Guillain-Barre Syndrome Association of NSW has a comprehensive website that explains the condition, outlines treatment and features Australian and overseas case studies. Its web address is gbsnsw.org.au. Telephone (02) 9869 1829 or email info@gbsnsw.org.au