published in Reader's Digest,
24 November 2023

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immunity [2] drug [3] wonder [4]



Mysteries remain about how the immune system can short circuit and cause autoimmune disease—but new research may hold the key to treating conditions like cancer.

Your body is at war; your immune system is in endless battle against a host of enemies including bacteria, viruses, parasites and, more often than you would like or are aware, cancer cells. Thankfully, your white blood cells are 'cut-throat killer cells [5]' patrolling the body, ready to engulf, entrap or dissolve unwanted visitors. Sometimes, though, an immunological mistake is made and the immune system attacks healthy body cells, leading to autoimmune disease. Affecting approximately one in ten individuals, more than 80 such diseases [6] have been identified; the science behind them is helping doctors understand how we might harness our body's immune response to actually treat disease.

Me and not me

In military conflict, team sport, or your immune system, it's vital to know who is on your side, and who is not. As white blood cells roam the body, interrogating each and every cell, ready to deploy a deadly arsenal of killer chemicals and microbe-massacring machinery, it's essential that so-called 'self-cells' belonging to us are able to declare themselves safe, saying "I'm one of us".

In her book 'Immune', Dr Catherine Carver likens this process to border patrol forces checking passports, with self-cells showing the correct paperwork (in this case, markers on their cell membranes). "The immune system is taught a key skill we should all learn very early in life: tolerance," she writes.

It's a much bigger job than you might imagine, deciphering this difference, with billions of potential invaders [7] and about 100 trillion cells in the human body. Everything from chickenpox to cholera, typhoid to tetanus may enter in, and some look remarkably similar to self-cells. Tuberculosis is the world's deadliest infectious disease, having briefly fallen behind COVID-19. Thankfully you've got an army of soldier cells, with your body making 100 billion neutrophils [8] each day, and, when called for, more antibodies than there are stars in our galaxy. 'Natural killer cells' are another type of white blood cell; their name is apt, their role under-appreciated.

"We pass our existence within this warm wobble of flesh and yet take it almost entirely for granted," writes Bill Bryson [9]. He suggests celebrating the glory of our existence – and much credit's due to the immune system.

Mistaken identity

Professor John Dwyer in his book, 'The Body at War,' reflects on the "real miracle that is the rarity with which our sophisticated and complicated immune system makes a mistake". But sometimes it does, targeting your own tissues, and causing autoimmune disease.

Symptoms will vary depending on where damage is done: if it's your joints, rheumatoid arthritis results; if it's your pancreas, you develop type 1 diabetes [10]. A recent paper in the Lancet [11] listed 19 of the most common autoimmune diseases, with some more well-known than others: Addison's disease, ankylosing spondylitis, coeliac disease, child-onset type 1 diabetes, Graves' disease, Hashimoto's thyroiditis, inflammatory bowel disease (Crohn's disease or ulcerative colitis), multiple sclerosis, myasthenia gravis, pernicious anaemia, polymyalgia rheumatica, primary biliary cholangitis, psoriasis, rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus [12], systemic sclerosis, vasculitis and vitiligo.

New autoimmune diseases are being discovered. Professor Belinda Lennox, head of psychiatry at the University of Oxford wonders whether some cases of schizophrenia [13] might be caused by autoimmune attack of cells in the brain.

What triggers the body to misdirect its immune response remains a mystery. Recent reports suggest, for example, that multiple sclerosis might begin with infection by the Epstein-Barr virus (EBV), a virus that infects about 95% of people, usually causing no symptoms, though sometimes it causes glandular fever.

Mysterious science

In one study of 10 million young adults from the US military over 20 years, a small subset of people who developed MS were seen to have first been infected with EBV. The MS Society [14] says though that "it will be many years before we know whether preventing EBV infection could stop people developing MS. Most people infected with EBV don't develop MS, so even if EBV is usually required to trigger MS, it can't be enough to cause it by itself. We need to deepen our understanding of how EBV interacts with other risk factors like vitamin D and genes".

The mystery deepens as we study ever more seriously the science of autoimmunity. In one large scale scientific study [11] of 22 million individuals over almost 20 years in the UK, during which almost one million people were diagnosed with one or more autoimmune diseases, some weird and wonderful questions were raised.

Why, for example, does it seem that childhood-onset type 1 diabetes is more commonly diagnosed in winter and vitiligo (a long term skin condition) in summer? Why do some autoimmune disorders, such as lupus and thyroid disorders, appear more common in women? Why might people living in deprived areas be more likely to be diagnosed with Graves' disease, pernicious anaemia, rheumatoid arthritis and lupus? Could it be that diet, smoking, obesity and air pollution play a role in the development of these diseases?

Manipulating the system

Could your immune system be tweaked to fight illness? Boosted or enhanced to fight cancer? Suppressed to abate autoimmune attack? In his book, 'The Beautiful Cure', leading immunologist Professor Daniel Davis says that we have "already found ways to harness our natural defences to create breakthrough drugs and so-called immunotherapies that help us fight cancer, diabetes, arthritis and many age-related diseases". Describing the "breathtakingly beautiful inner world" that is our body, he says that the immune system is far more powerful than any medicine ever invented.

Targeting the immune system to fight cancer is a complicated, but not a crazy idea. Cancer cells appear throughout life, and your natural killer white blood cells often (but not always) recognise when cells go wrong in this way and destroy them. Anti-cancer immunotherapy [15] can help amplify this existing immune response. Also called

targeted treatment or biological therapy, immunotherapy is not suitable for all cancers but is, for some, one of the main treatments; types include monoclonal antibodies and CAR-T cell therapy.

A reduction or suppression of the immune response is required when there is autoimmune attack on an organ - and when there is an unnecessary immune response in allergy [16], or when there is rejection of an organ after transplant. So-called suppression immunotherapy [17] is useful here.

That we can 'turn up', or 'turn down', the immune response to fight disease opens up a whole new chapter in medical textbooks and for some patients, there might just be a happy ending.



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