

From the library

Remembrance of things past

"Marcel and Robert were impatient to leave the train when it stopped briefly at the small station. The Parisians usually walked to the Amiets' house from the station, carrying the blankets that kept them warm on the train, along with their parcels and suitcases down the rue du Chemin de fer, lined on both sides with linden trees. Turing left at the rue de l'Oiseau flesché, they passed in front of the ancient hostelry of the same name. Marcel always noticed the optician's sign consisting of a large pair of spectacles, one lens blue, the other orange, unaware that one day he would transport these glasses hanging high above the optician's shop into the fictional Combray, where they became a symbol of his book and his conception of the novel." (Carter WC. *Marcel Proust*. New Haven: Yale University Press, 2000:26.)

Shifting emphasis at the WHO

It all started with a 1996 report by Christopher Murray of Harvard School of Public Health and the World Health Organisation, and WHO researcher Allan Lopez. Investigating the health problems of the world's population, these investigators shifted their emphasis from simply tabulating the greatest killers to those diseases that produced the greatest burden on society. This, not surprisingly, led to a much greater emphasis on chronic diseases such as cancer and mental illness. Moreover, this report predicted that by the year 2020 non-communicable diseases would cause 73% of all deaths worldwide, and only a minimal number of deaths would be a result of infectious disease (15%).

As a result, there is now a shift in the priorities of the WHO towards non-communicable diseases. This is partly based on the notion that increasingly people in the developing world are leading the same, perhaps some would say destructive, western lifestyles. Although this means less child mortality, it means more adults die of cancer and heart disease.

Tension exists between different members of the WHO as to how far this shift in resources away from non-communicable diseases in the third world should go. Some even point out that infectious disease may increase as the result of some of our ecological problems. For example, global warming allows insect borne diseases such as dengue and malaria to spread. Regrettably, the all too common refugee camp seen in so many poor parts of the world obviously provides a breeding ground for infectious disease.

The example of the AIDS epidemic and its other infectious disease crisis, drug resistant tuberculosis, only reminds us that, while infectious diseases worldwide may be decreasing in their significance, they still remain a major threat to the health of a significant portion of the world's population. (*New Scientist* 1 April 2000;165(No 2232):16.)

Infectious agents and chronic diseases

In the past decade, a growing body of evidence has challenged our previous notions of the pathophysiology of certain diseases. For example, it now seems clear that in the case of peptic ulcer disease and perhaps in coronary artery disease infectious agents may have an important role in the genesis of these disorders. Now there seems to be additional evidence to challenge our classic notion about the so called autoimmune conditions. These conditions like rheumatoid arthritis, myasthenia gravis, and multiple sclerosis have usually been considered to be diseases in which the lymphocytes of the patients undergo mutations and produce immune responses which attack their own tissues. An alternative theory suggests that molecular mimicry may be the basis of these disorders. This theory is based upon our understanding of rheumatic fever. In this disorder, anti-streptococcal antibodies bind to cardiac and muscle tissues (as well as to brain tissues) because there is molecular similarity between these tissues of the patients and the streptococcal antigens. As the result of antibody binding at a particular site a series of reactions by a group of proteins called "complement" is activated that leads to destruction of the involved tissues. In the case of rheumatic fever, widespread use of antibiotics against streptococcal infections has virtually eliminated the threat of rheumatic fever in the Western world.

Now it appears that similar molecular mimicry may be important in ankylosing spondylitis and rheumatoid arthritis. There is some evidence to suggest that *Klebsiella* participates as the molecular mimic in ankylosing spondylitis whereas in the case of rheumatoid arthritis it may be the *Proteus* bacterium.

The molecular mimicry theory has been expanded to challenge the prion hypothesis in the case of bovine spongiform encephalopathy. In this case, there is evidence to suggest that cattle exposed to *Acinetobacter* develop bovine spongiform encephalopathy, as the result of molecular mimicry of this infectious agent and bovine brain tissue. If *Acinetobacter* bacteria actually evoke the immunological response that provokes the pathological alterations in the proteins of the involved neuronal cells the antibodies produced might act as antibodies and the prion theory would therefore be irrelevant. (Ebringer A. Molecular mimicry, mad cows and arthritis. *Science Spectra* 2000;19:46.)

The biochemistry of memory and learning

Although the project to raise genetically engineered smarter mice has been the subject of ridicule by David Letterman on his CBS late show, this scientific project has significantly enhanced our understanding of the molecular

machinery responsible for learning and memory. These mice have been genetically engineered to make more than the usual amount of a key subunit of a protein called the N-methyl-D-aspartate (NMDA) receptor. This receptor helps to strengthen the connections between two neurons that are active at the same time. In the genetically engineered mice, the NMDA receptors stay open nearly twice as long as in normal mice and this seems to correlate with their enhanced memory capability. The NMDA receptor is essentially a pore that allows calcium to enter the nerve cells—calcium being a prerequisite to strengthen the connection between two cells.

For the past several years several pharmaceutical companies have been investigating compounds that might decrease the activity of the NMDA receptor for the treatment of stroke. This seems almost counterintuitive if the NMDA receptor is important for memory and learning. However, this theory can be understood by realising that as the result of hypoxia nerve cells release too much glutamate, a chemical that binds to the NMDA receptor on the nerve cells and promotes a cascade of calcium to flood into it from other cells. Coupled with hypoxia this causes the cell to die. Thus, ironically, NMDA receptor inhibitors might be useful in the treatment of ischaemic brain disease while at the same time NMDA receptor facilitators might be useful in the treatment of dementing brain disorders. (Tsien JZ. Building a brainier mouse. *Scientific American* 2000;282:62.)

Recommended reading

Genome: The Autobiography of a Species in 23 Chapters. By Matt Ridley. New York: Harper Collins, 2000.

An ugly battle is being waged between the private company Celera Genomics and the US government's National Human Genome Research Institute. Both bodies are engaged in a race to map the entire human genome. Other companies in genomic research that have invested in this race were severely affected when President Clinton commented that he might oppose allowing research based on the human genome data to be patentable. The high flying American stock market reacted in a predictably negative way. In a new book written by Matt Ridley, a scientific writer, the background of the human genome project is merged with a well written summary of our current understanding of human genetics. Ridley covers a broad range of topics including the genetic basis for ageing and immortality, population genetics, as well as the recent evidence for genetic links to memory, intelligence, personality, language, and even free will. The book is marred by occasional flights of fancy and overenthusiasm by the author, but it is a clear and well written discussion of a topic of increasing interest.



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