From the library

Remembrance of things past

As a young man, he would become famous for conducting with closed eyes. This was partly to avoid visual distractions, but as he would later explain: "After I learned a score, at the end I try and forget what I've seen, because seeing and hearing are two such different things." It would be untrue to say that Karajan had a deficient visual sense; he was obsessed with stage design and stage lighting. But as often as not, the outcome of a hundred Karajan lighting rehearsals would be what the poet Milton calls "no light but darkness visible". Several key works which held Karajan enthralled for most of his life—Wagner's *Tristan und Isolde*, Debussy's *Pelleas et Melisande*—inhabit closed worlds, womb like in their darkness and seclusion. (Osborne R. *Herbert von Karajan, A Life in Music*. Boston: Northeastern University Press, 2000:7–8.)

Antibiotic inhibits brain cell death

In Huntington's chorea, a faulty gene makes brain cells commit suicide on mass. The antibiotic minocycline prevents some of this process by inhibiting key enzymes called caspases that initiate programmed cell death. The drug may also slow cell death in other conditions such as Alzheimer's disease and strokes. (*Nature Medicine* 2000;**6**:797.)

Virus treatment of brain tumours

Researchers in Scotland have shown that a strain of herpes simplex virus (which causes cold sores) can be used to selectively kill tumour cells in gliomas, the most aggressive form of brain cancer. A strain called HSV1716 destroys only tumour cells, leaving healthy brain tissue unharmed. In none of the patients treated thus far have adverse reactions been reported; the virus did not establish a permanent infection, or spread throughout the body. Encouraged by these results, the researchers plan to initiate further trials by the end of the year with testing of this therapy on patients with the skin cancer melanoma as well. (*New Scientist* 2000;**2246**:17.)

Infants' motion asymmetry and strabismus

Normal young infants (but not neonates) exhibit nasotemporal asymmetry when measured by optokinetic nystagmus, pursuit movement, or visual evoked potentials (VEPs). A similar asymmetry of motion processing has been reported in patients with early onset esotropia. Whether this asymmetry is merely an epiphenomenon or is an expression of the abnormal neural substrates in strabismus is not yet known. In this study, motion VEPs were recorded from healthy term infants as well as infants with esotropia. Neonates did not exhibit motion VEP asymmetry. Normal infants, 2–3 months old, exhibited marked nasotemporal asymmetry, which diminished by 6–8 months. Regardless of the age at surgery, most patients with infantile esotropia had persistent asymmetric motion VEPs after surgery. The data from this study support a strong link between fusion and motion VEP symmetry during both normal maturation and infantile esotropia. Furthermore, the finding that paediatric patients with infantile esotropia do not differ significantly from normal immediately after the onset of strabismus suggests that the nasotemporal asymmetry found in such patients may not represent a persistence of the normal infantile state, but rather a pathological disruption of motion pathways as a result of prolonged abnormal binocular sensory experience. (Birch *et al. Investigative Ophthalmology and Visual Science* 2000;**41**:1719–23.)

Sugars and the aging process

Sugars are an essential source of energy but once in circulation they act as molecular glue, attaching themselves to the amino groups in tissue proteins and cross linking them into hard yellow brown compounds known as advanced glycation end products. The premature ageing that occurs in diabetic patients and in experimental animal models has been cited as further evidence to suggest that the effects of sugars may be important in the long term ageing process.

In the mid 1980s, Anthony Cerami, of the Kenneth Warren Laboratories, demonstrated that amino acid guanidine could keep the tissues of diabetic rats and other old animals as elastic as those of young control animals. At a recent symposium in London, Cerami reported the use of a chemical (ALT-711) that can reverse the increased glycanation process that produces stiffness in the heart, joints, and arteries of these animals. Although other processes are known to be important in the ageing process—for example, free radical oxidation and possible telomere shorting, research on chemicals to inhibit advanced glycanation end products seems promising. (*Scientific American* 2000;**283**:16.)

Brain cell growth in adults

Neurobiologists long believed that adult brains did not make new neurons, we now know otherwise. Investigators have reported the birth of new neurons in the hippocampus of adult rats, monkeys, and humans. Preventing depression may depend upon proper control of this ongoing neurogenesis. Apparently, in most parts of the adult brain, something inhibits progenitor cells from dividing to produce new neurons. But in the case of those cells in the hippocampus, a steady neurogenesis occurs throughout adulthood. Now scientists are stressing the possibility that depression may result from inhibition of this process and the resulting decrease in hippocampal volume. Moreover, antidepressant medications may work by stimulating this normal neurogenesis process to resume. In this case serotonin appears to be important in the neurogenesis process but other means of increasing neurogenesis may be identified and have clinical relevance. (*American Scientist* 2000; **88**:340–6.)

Anti-inflammatory drugs and Alzheimer's disease

In the early 1990s investigators at the Sun Health Research Institute in Sun City, Arizona, noted a startlingly low occurrence of Alzheimer's disease in patients with arthritis. Since that time, multiple studies have demonstrated that patients who take anti-inflammatory drugs (aspirin or non-steroidals) for chronic disorders seem to suffer from a much lower rate of Alzheimer's disease than those patients who do not use these drugs chronically.

Doctors Patrick and Edith Mageer have now offered a plausible theory of why anti-inflammatories might be effective in reducing or at least delaying the onset of Alzheimer's disease. The characteristic plaques and tangles that are found in the brains of patients with Alzheimer's disease are filled with compounds especially the protein β amaloid that can promote the brain's innate immune system. This may, in turn, promote the migration and activity of the microglial cells of the brain, which begin producing toxins that cause further damage to unaffected neuronal cells. This further cell damage promotes even more inflammatory response, which continues the vicious cycle of neuronal death. Interrupting the inflammatory cascade may at least minimise some of the subsequent inflammatory induced neuronal death. Moreover, the drugs dapsone (an anti-inflammatory used for decades to treat leprosy) and the so called COX-2 inhibitors appear to be free of the major side effects of other anti-inflammatories, especially gastrointestinal bleeding, and yet appear likely to be effective in inhibiting the inflammatory neuronal death induced in Alzheimer's disease. (*Scientific American* 2000;June:24.)

Immunotherapy for melanoma?

Surgery, chemotherapy, and radiation are the standard treatments for cancer. Melanoma is relatively resistant to chemotherapy and radiotherapy, but appears to respond well to a variety of immunotherapies. Melanoma is therefore a good model for improving the understanding of the immune response to cancer. A variety of mechanisms generating T cell epitopes on tumour cells have been discovered in melanoma treatment. New immunisation protocols including immunisation with peptides, recombinant viruses, plasmid DNAs, and dendritic cells pulsed with peptides as well as adaptive transfer of in vitro generated cytotoxic T lymphocytes by stimulation with antigenic peptides have been developed. Immunisation with the gp-100 peptide modified to have high HLA-A2 binding affinity has a resulted in a 42% response rate in patients with melanoma. (Kawkmi Y. New cancer therapy by immunomanipulation. *Cornea* 2000;**19**:s2–s26.)