From the library

Remembrance of things past

Frankly, given our aesthetic propensities, we would not always wish to perceive these smaller worlds within our domain. About forty percent of humans house eyebrow mites, living beneath our notice at the base of hair follicles above our eyes. By ordinary human standards, and magnified to human size, these mites are outstandingly ugly and fearsome. I would just as soon let them go their way in peace, so long as they continue to favor utter imperceptibility. And do we really want to know the details of ferocious battles between our antibodies and bacterial invaders—a process already distasteful enough to us in the macroscopic consequences of pus? (Don't get me wrong. As a dedicated scientist, I do assert the cardinal principle that we always want to know intellectually, both to understand the world better and to protect our selves. I'm just not sure that we should always crave visceral perception of phenomena that don't operate at our scale in any case.) (Stephen Jay Gould. *The living stones of Marrakech: penultimate reflections in natural history*. New York: Harmony Books, 2000:355.)

Drug compliance and tuberculosis

The problem of patient compliance in completing prescribed drug treatment in medicine is well appreciated. It is a particular problem in the case of tuberculosis. The World Health Organization has warned that the bacterium responsible for tuberculosis is becoming resistant to antibiotics because of the failure of patients to complete their course of treatment. A new procedure mixes the antibiotic with a fluorescent dye (indocyanine green). When the skin is illuminated the fluorescent dye causes a slight fluorescence of the skin. Patients wear a bracelet that shines light at the skin and doctors can immediately detect by the presence or absence of fluorescence whether the patient is taking the medication. (*New Scientist* 2000;2260:7.)

Altering the mosquito to prevent malaria

Nearly two million people die as the result of malaria each year. Therefore, malaria ranks second only to tuberculosis as the deadliest communicable disease. Current treatment of malaria is the use of quinine derived drugs. However, rapid mutations taking place in the malarial genome will soon make these antimalarial drugs ineffective. Devising an effective vaccine against malaria is an important goal. However, immunologists have not yet developed an effective long term prophylaxis for parasites as complex as plasmodia. Thus, an alternative form of preventative therapy for malaria is being investigated. A research team, at Imperial College of Science, Technology and Medicine in London, has taken the first important step to genetically alter the carrier of malaria, the *Anopheles* mosquito. This team has successfully introduced a new strand of DNA into the mosquito genome. The next step is to try to insert genes that express malaria specific antibodies into mosquito body parts, such as the salivary glands and the gut, that harbour the plasmodium parasites. (*The Sciences* 2000;**40**:10–11.)

Help for the colour blind

Two recent developments in technology may prove useful for the segment of the population that has one of the many forms of congenital colour blindness. The first developed by the Hokkei industry in Japan, is a scanning device, which reads the colour of any object. It will also provide several modifiers of intensity of colour in its description. This would allow colour blind patients to scan their clothes. Regrettably this technology is only available at the present time in a Japanese language form. A software package developed in Pittsburgh, Pennsylvania, that has been referred to as a colour deficiency simulator allows product designers to perceive the world in ways that colour blind patients do. The idea is for designers to avoid colour construction that might be confusing for the colour blind patient. At the present time this software is only available for the three most common forms of congenital colour blindness. (*New Scientist* 2000;2260:12.)

Imprinted genes and fetus size

Ordinarily, embryos receive two copies of each gene: one paternal and one maternal. Usually the genes in a pair behave exactly the same way. However, so called imprinted genes are different. They have a methyl group that instructs them to be active or inactive depending on which parent they come from. Recent investigations suggest that imprinted genes for a growth hormone called Igf2 (insulin-like growth factor 2) may be responsible for determining the size of the developing fetus. Igf2 produces larger fetuses and is active only when it comes from the father. When the Igf2 DNA is missing, mutant mice fetuses are 30% smaller than when it is present. (*Scientific American* 2000;**283**:25–6.)

Blind patients and auditory perception

Blind and sighted volunteers were studied electroencephalographically to investigate whether there was a difference in auditory processing between the two groups. The N400 signal was measured on the EEG in both groups while they listened to sentences in which the last word either did or did not make sense. The N400 signal is thought to correlate with semantic processing. In the sighted volunteers, this signal appeared at about 150 ms after the sentence had ended. However, in blind volunteers, the N400 signal occurred at approximately 75 ms. This suggests that blind patients process auditory information more quickly than the normal sighted person. This study also documented that electrical signals over the visual cortex in blind patients appeared to be involved during auditory processing suggesting perhaps that portions of the visual cortices were being utilised in auditory activities. (*Neuropsychologica* 2000;**38**:1482.)

Neuronal death in degenerative brain disease

Heretofore, it has been widely believed that neuronal death in the central nervous system occurs according to the accumulative hypothesis. In this hypothesis cells affected by neurodegenerative diseases become sensitive to various biochemical stresses that lead to the formation of fibrils and the production of free radical molecules. At low levels, these may be tolerated but eventually the concentration of fibrils and free radicals will overwhelm the neuron and death will occur. In this model the probability of a neuron dying increases over time as it is exposed to the damaging effects of stress. This cumulative death hypothesis therefore suggests that the change in the percentage of healthy neurons over time stays relatively flat until a dramatic falloff occurs.

Recent studies in Toronto challenge this thesis. Using data obtained from 10 previous studies of illnesses such as vision impairment, Parkinson's disease, and Huntington's disease, these investigators concluded that neurons in these disorders did not die in a pattern consistent with accumulative death hypothesis. In other words, there was no dramatic sudden loss of the neuronal population. The authors suggest that neuronal death occurs as a catastrophic event or in a one hit hypothesis. Two important therapeutic implications of this hypothesis might lead to better treatment of neurodegenerative diseases. (1) Therapies could halt the progress of disease by keeping the damaging effect of the fibrils below a threshold level. (2) The one hit model suggests that the probability of rescuing neurons does not decrease with age. Therefore, effective treatment for diseases like Alzheimer's and Parkinson's disease should be effective for patients who already show significant neurological handicap. (*Scientific American* 2000;**283**:26–7.)

Therapeutic options for glaucoma

Glaucoma experts recently met at Juan-Les-Pins, France, to discuss the therapeutic options for glaucoma. There now seems to be consensus among glaucoma experts that, while reducing intraocular pressure is still the most important step in treating patients with glaucoma, lowering intraocular pressure alone may not be sufficient in the treatment of all glaucoma patients. Two new drugs developed by Allergan may address directly the mechanisms that underlie damage to the retinal ganglion cells in glaucoma.

Brimonidine (Alphagan) is currently available for the treatment of glaucoma. In addition to its intraocular pressure lowering effect, this drug also seems to protect the retinal ganglion cells by upregulating proteins such as basic fibroblast growth factor through an endogenous intrinsic survival system. In a glaucomatous rat model, brimonidine reduces retinal ganglion cell loss from 33% to 15% over a 3 week period.

More promising is memanitine, a drug currently undergoing studies in patients. Memanitine blocks the NMDA receptor on retinal ganglion cells. The NMDA receptors are susceptible to the action of glutamate, which promotes changes in retinal ganglion cells as part of a cascade of neurotoxic events promoting cell death. Recent animal studies show a 75% reduction in glaucoma induced loss of retinal ganglion cells with the use of memanitine. (News release from Allergan Europe.)