are only used in research when it is absolutely necessary. They are highly intelligent creatures and the decision to use them in a scientific study is not taken lightly. Under the 1986 Animals (Scientific Procedures) Act, cats, dogs and NHPs are afforded special protection and in 2002 were collectively used in less than 1% of the 2.73 million procedures in the UK.

Scientists that use animals face a number of practical issues in addition to intimidation and physical threats. These include the lengthy processes required by law to obtain and amend licenses for animal experimentation, and the supply of the animals themselves.

Almost all NHPs used in the UK (macaque monkeys and marmosets) are obtained from captive-bred breeding colonies. They have known family histories and are supplied with health profiles from birth to shipment. The majority of macaque monkeys are bred and weaned in their countries of origin, which means that the animals have to endure lengthy transportation periods. When they are shipped to the UK, careful consideration is given so that those animals that have grown up together are transported together, as a result they can be acclimatized to their new surroundings with animals that they know.

The green light?

However, a spokesperson from a leading UK research company told *BioMedNet News* (http://news.bmn.com) that as a result of animal rights groups targeting airline carriers, it is nearly impossible to transport animals directly into the UK. 'Different transportation mechanisms have been introduced to overcome this situation, along with additional feeding stations to minimize the stress to the animals. But this increase in transit time that directly results from animal rights targeting, has effectively compromised animal welfare. Both the time taken to obtain licenses and animal importation issues have caused some primate researchers to relocate their studies to the USA.'

As for Cambridge University, while they finally have permission to build their new neuroscience centre, the escalating costs due to the three-year wait mean that there is no guarantee it will go ahead.

Private prescription:

A thought-provoking tonic on the lighter side

Column by Raymond C. Rowe, AstraZeneca, UK

Please note that these are the personal opinions of the author and do not necessarily represent those of AstraZeneca.

A spectrum of limericks

Invariably in physical chemistry textbooks you will find a section on the electromagnetic spectrum detailing the distribution of electromagnetic waves according to their frequency and wavelength. The various frequency ranges are characterised by the different behaviour in the emission, transmission and absorption of the waves. From the shortest to the longest wavelength (the highest to the lowest frequency), frequency ranges include gamma-rays, X-rays, visible light, heat and infrared and radio waves. Methods of detection vary but include, photography for the short and medium range of wavelengths, bolometry for the infrared region and crystal detectors, vacuum tubes and transistors for the radio waves.

The study of these waves has spawned many Nobel Prize winners for physics, not least Wilhelm Röntgen in 1901 for the discovery of X-rays, Henri Becquerel, Pierre and Marie Curie in 1903 for work on radiation, Guglielmo Marconi in 1909 for the development of wireless telegraphy, and John Bardeen, Walter Brattain and William Shockley in 1956 for the development of the transistor. All of these scientists and their discoveries have been celebrated in limericks. Indeed the electromagnetic spectrum has resulted in a spectrum of limericks.

Gamma-rays

In March 1896, Antoine Henri Becquerel began looking for a crystalline substance that emitted penetrating radiation of similar properties to X-rays, which had been discovered by Röntgen a few months earlier. Becquerel found that luminescent and non-luminescent compounds of uranium made records on a photographic plate wrapped in black paper, even though the specimen

PII: S1359-6446(03)03012-5

and plate lay in total darkness. In May 1896, Becquerel found that a disc of pure uranium also produced these penetrating rays, and this discovery of radiation was established, as stated in the limerick [1]:

Becquerel was having a go,
At what made substances glow,
With uranium he played,
And discoveries he made,
But that was the end of his show.

At about the same time Marie Curie chose to study the radiation from uranium for her doctoral thesis. Working with her husband Pierre, Marie found that uranium ore was more radioactive than uranium and subsequently extracted polonium and radium. Pierre published two papers on the physiological action of radium rays after subjecting his arm to a burn and studying their toxic effects on mice and guinea pigs. The Curies were concerned by these effects, as so aptly noted in the limerick [1]:

'The electromagnetic spectrum has resulted in a spectrum of limericks.'

Madame Curie loved Pierre,
And together found elements rare,
But they stood way too close,
And got quite a dose,
And suffered from falling of hair.

X-rays

X-rays were discovered in November 1895 when Wilhelm Röntgen was experimenting with high voltage current in an evacuated glass bulb. Within two months he had completed his investigations, written a detailed paper and taken several X-ray photographs. Newspapers hailed the discovery, and within a few months X-rays were being used in clinics to detect foreign bodies in patients and to help in setting bones. The following limerick sums this up perfectly [1]:

The integument used so to hide
The organs and bones deep inside
'Till Röntgen discovered
Rays that uncovered
Whatever was wounded, save pride.

Photography

Photography as we know it today emanated from the recognition in the early eighteenth century that the blackening of silver salts was caused by light and not, as was first thought, by heat. Although the first photograph using a camera was achieved in 1826 by the French lithographer Joseph-Nicéphore Niepce, it was Louis-Jacques-Mandé Daguerre, a French scenic painter, who in 1839 published a detailed description of the first commercial process. The daguerreotype process, as it was known, used a camera to expose a silver plated sheet of copper pre-treated with iodine vapour. The image was then developed with mercury vapour and fixed with sodium chloride. The process and its inventor are celebrated in the limerick [2]:

Exposing his plate to the air,
Did its clever inventor declare,
"C'est venue – ma photo,
Complète – in toto-
C'est magnifique – Je suis Daguerre!"

Unfortunately, although used extensively for a few years, the process proved to be a dead end in the development of photographic technology.

Infrared rays

In the late nineteenth century there was a growing interest in solar activity and its influence on the weather. To study the solar spectrum into the infrared region, in 1878 the American physicist Samuel Langley invented a radiant heat detector that was sensitive to differences in temperature of one hundred-thousandth of a degree. The invention, together with a comment on its sensitivity, is celebrated in the limerick [3]:

Oh Langley devised the bolometer.
It's really a kind of thermometer
Which measures the heat
From a polar bear's feet
At a distance of half a kilometre.

Radio waves and transistors

The assertion that electromagnetic waves travelled in straight lines and could be reflected just as light is reflected by a mirror was first demonstrated in 1888 by Heinrich Hertz. However, it was not until six years later that Guglielmo Marconi, using a relatively crude apparatus, succeeded in transmitting and receiving radio waves over distances of two kilometres. Following further developments in the apparatus, signals were transmitted across the Atlantic Ocean in 1901. Additional modifications to Marconi's transmitter (the sparker), and the subsequent discovery of the crystal rectifier (a piece of galena with a cat's whisker probe) by Ferdinand Braun, led to even greater improvements in radio wave transmission, and resulted in Marconi and Braun receiving the 1909 Nobel Prize for physics. However, as the limerick records [1], Marconi is the one accorded fame:

Marconi sent signals through air,
On waves of which Hertz was aware,
With sparkers and bristles,
On galena crystals,
'Till radios were found everywhere.

In another limerick [2], Marconi's personal attributes are mentioned (he was an unabashed womaniser):

Marconi, whose ardour was tireless,
Sat down and invented the wireless,
Which makes it less tough
For the musical buff
Who lives in a town that is choir less.

The limitations of vacuum tubes (bulkiness, high power consumption, fragility and short life) soon stimulated research into alternative devices to rectify and amplify signals. In 1948, the invention of the transistor was announced by Bell Telephone Laboratories, which resulted in the 1956 Nobel Prize for physics being awarded to John Bardeen, Walter Brattain and William Shockley. The limerick [1] celebrates their invention (the word rube in the penultimate line is slang for an unsophisticated, uncouth person):

Schockley, Brattain and Bardeen,
Commanding electrons unseen,
Made vacuum tubes,
Fit only for rubes,
And those who think progress obscene.

Final analysis

As I have intimated in similar previous articles, the limerick offers an ideal way of presenting science and scientific concepts. In this case, my examples all relate to the theme of the electromagnetic spectrum and in themselves provide a spectrum of detail and information on the discovery and the inventors and scientists involved. It is interesting to note that the scientific limerick has not lost its appeal. Far from it, my collection is growing by the month, although the field of drug discovery and development is still lacking examples!

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In vitro experimental models for the blood–brain barrier

In recent years, *in vitro* experimental models have been widely accepted and applied in drug development. Artificial membranes [e.g. parallel artificial membrane permeability array (PAMPA)] and various cell-based models (e.g. Caco-2) have greatly facilitated the screening of molecules for intestinal permeability. Liver microsomes and hepatocytes are routinely used in the evaluation of metabolic fate (e.g. metabolite identification), metabolic stability and drug–drug interaction potential (e.g. P450 inhibition and induction). Hepatocytes and liver cell lines are commonly used to screen for hepatotoxic potential. These *in vitro* assays greatly facilitate the drug development process because they enable the optimization of drug candidates with appropriate drug-like properties [1].

One area that is lagging behind is the development of a practical blood–brain barrier (BBB) model. The BBB serves as a physiological protective barrier between the central nervous system (CNS) and the systemic circulation. For CNS drugs, ready penetration across the BBB is necessary for efficacy. For non-CNS drugs, non-permeability is preferred to minimize CNS toxicity. Non-permeability is especially important for cytotoxic drugs (e.g. anticancer agents). Therefore, an *in vitro* experimental model that can accurately predict drug BBB permeability in humans will greatly enhance drug discovery and development.

In vivo, the BBB is represented by tight junctions between the endothelial cells of the microcapillary and the glial processes that form ‘endfeet’ surrounding the microvessels. The barrier thereby consists of the cell membranes of the non-fenestrated endothelial cells and the glial cells, and their respective tight junctions. Furthermore, the endothelial cells possess highly effective drug efflux systems [2], such as the P-glycoprotein (Pgp), which serve to remove xenobiotics that have entered the endothelial cells. A drug that can effectively penetrate the BBB is one that can penetrate through the endothelial cells and glial processes and is not removed from the endothelial cells by the drug efflux mechanisms.

It is now widely accepted that BBB models require the participation of multiple cell types: the brain

PII: S1359-6446(03)02877-0