development of quantitative techniques for the measurement of receptor pharmacology[12,13]. This work was stimulated by many elegant demonstrations of binding of specific radioligands to receptors in tissue homogenates or slices.

The transition from quantitative *in vitro* binding studies to *in vivo* examination with PET is complex. *In vitro*, binding affinity and number of binding sites are analysed under strict equilibrium conditions which are easily achieved. *In vivo* studies have to be made under non-equilibrium conditions brought about by factors which affect the regional concentration of free radioligand in the brain, such as nonspecific binding of tracer in blood and brain, blood–brain barrier permeability and blood flow. The metabolism of the tracer can also cause various radiolabelled metabolites to appear in both blood and tissue. As a result, quantitative estimates of the number of receptors and their affinity cannot be obtained from a single measurement; rather, multiple sequential measurements, easily obtained with PET, are needed to delineate the time course of the radioactivity both in the tissue of interest and in the blood, with a correction for the presence of labelled metabolites in the blood.

The data must then be analysed using an appropriate mathematical model to relate brain and blood radioactivity measurements to measurements of receptor physiology. Inferences drawn from qualitative, *in vivo* measurements based on single tissue autoradiograms or PET images must be viewed with extreme caution, despite their intuitive visual appeal. Unfortunately this sort of inference is the rule rather than the exception.

Recent attempts to examine the more complex but equally interesting subject of transmitter metabolism with PET have suggested another fruitful area of research[24]. All the complex issues facing the study of receptor pharmacology also apply here, with the added problem that local tissue metabolism of the radiolabelled tracer is especially critical. Considerable time, effort and money will be necessary to perfect such measurements but current evidence suggests they will be amply rewarded.

A thoughtful review of PET research clearly indicates it is gradually fulfilling its promise as a legitimate and important tool for clinical research. Considerable uneveness in the quality and quantity of published research from extant PET centres is, however, very evident. What are some of the problems? One factor is clearly a normal process of maturation of a very complex technology, one which is simultaneously advancing on several important fronts. Initial development is necessarily slow — particularly as instrument design and construction, radiopharmaceutical development and tracer modelling, as well as experimental design, execution and interpretation have often all had to occur in a single PET laboratory. For success, this process requires interaction and close collaboration between investigators with expertise in instrumentation, chemistry, tracer kinetics, clinical neurology and neurobiology: full commitment is essential. Workers in this field would now agree this is not easily or quickly achieved, which perhaps accounts

John F. Enders (1897–1985)

John Enders, who died unexpectedly on 8 September 1985 just as he had finished reading a volume of poems by T.S. Eliot, was awarded a Nobel Prize for Physiology and Medicine in 1954 for discovering how to grow the poliovirus in culture, which was crucial to the development of the first polio vaccine.

Enders had an almost lifelong scholarly interest in English and Celtic literature, and it was while working on a doctoral thesis about the use of gender in Middle English that he became interested in microbiology. He was sharing rooms with H.K. Ward, who had come from Australia to work with Hans Zinsser and Enders's long-latent interest in biology was roused by his visits with Ward to Zinsser's laboratory. Consequently, when he did obtain a Ph.D. from Harvard University in 1930, his thesis concerned the purification from the tubercle bacillus of the carbohydrate antigen that caused anaphylaxis and was separable and distinct from the protein antigen that caused delayed hypersensitivity. Like most microbiologists of his generation, Enders studied the tubercle bacillus and the pneumococcus in the search for improved serum therapy. In 1933, his classic paper with Ward showed that the opsonic activity of serum against type II pneumococci was due to specific antibody and complement.

His interest in virology resulted from a devastating epizootic in kittens that swept through the animal quarters of the Harvard Medical School in 1937. He quickly discerned that the cats had a disease that a filterable agent could transmit. His publication in 1939 on distemper in cats must be a landmark in the clinical feline literature for it describes in clear and concise detail the clinical course, the pathology and the aetiology of the disease. He became interested in the problem of *in vitro* propagation of viruses and, in 1940, reported with A.E. Feller and T.H. Weller the first successful prolonged culture of a virus in roller-tube cultures. These promising leads on the cultivation of vaccinia virus, and subsequently influenza virus, were interrupted by the outbreak of the Second World War. In 1941 he became a consultant to the Secretary of War on epidemic diseases. A massive plasma fractionation programme was being developed in E.J. Cohn's laboratory at the Harvard Medical School and Enders showed that antibodies to a variety of antigens were not fractionating uniformly. He anticipated the future discovery of IgM, IgA and IgG antibodies. At the war's end, he took up a detailed study of the mumps virus; he purified the complement-fixing antigen from parotid glands of infected monkeys, developed the skin-test material for eliciting delayed hypersensitivity in immune individuals and eventually he managed to propagate the mumps virus in tissue culture.

While this work was progressing, he moved his laboratories from the Department of Microbiology at the Harvard Medical School to the nearby Children's Hospital. There he was joined by T.H. Weller and F.C. Robbins. In 1949, they jointly reported in *Science*, in the briefest and most understated terms, the sensational finding that they had succeeded in propagating the poliovirus in tissue cultures of non-neuronal origin. They measured a 10^{15}-fold increase in infective virus during the period of culture as assayed by mouse intracerebral inoculation. Within the year, they were able to circumvent this cumbersome bioassay by observing a cytopathic effect on human foreskin fibroblasts *in vitro* as revealed by changes in *p*H in the culture fluid. In three brief, concise reports, the groundwork was laid for the development of a vaccine that has relieved untold amounts of human deformity, suffering and death. In 1954, Enders was awarded the Nobel Prize for this discovery but declined to accept the honour unless his two young colleagues, Weller and Robbins, who, as he said, "had done the work", could also share the prize. And so they did. This must be the most unsordid act in the history of the Nobel Prize and betrays the humbleness, decency and modesty which characterized the life of John Enders.

In the following summer, ironically, Boston was struck by the most devastating polio epidemic in its history. By this time others were busily engaged in polio vaccine development, so Enders turned his attention to the measles virus and successfully developed a measles vaccine. In his last decade of work, he made important contributions to the transformation of cells *in vitro* by simian virus 40 and the oncogenicity of these transformed cells in hamsters. He finally ended his active work in 1972 at the age of 75.

John Enders was in many ways a richly endowed man and he shared these gifts with many people. He was descended from a family that had great success in the insurance and banking businesses but he eschewed a life of ease, or one in the financial world, after a brief and unsuccessful attempt at it in 1920. He felt that his roots lay with Edward Jenner and Louis Pasteur, whose picture always adorned his office. In this he was correct. F.S. Rosen

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