NUCLEAR MEDICINE

Experience should teach me that one should never promise to any editor to write a contribution for his or her journal within two weeks of the initial encounter. It can only be explained via the smoothing influence of a Christmas visit that one is caught in making such precipitated offers. There we are, and we now have to live up to our promise.

Nuclear Medicine (or as it has been defined, the last refuge for the practice of internal medicine) remains indeed an exciting subject. It also remains one of the most misunderstood medical subjects of our time. Whilst the excitement is easy to explain, the misunderstanding (as always) is the outcome of historical events and the complex issues which surround the peaceful application of nuclear energy to the benefit of mankind. The most basic concept of radioactivity remains completely shrouded in mystery and fear by large segments of even to so-called *informed* population and naturally by most people at large. The international agencies and national organisations have failed to put across to the layman and woman the true nature of radioactivity (which is a natural phenomenon), the risks involved and the possible benefits. It is common practice for hospital ethical committees (in those hospitals where such institutions form an integral part of hospital life) to shrink from a true assessment of the risks involved in the medical application of radionuclides, and this is largely due to pure ignorance of the factors involved. By contrast, radiological techniques, involving in general terms much larger exposures to patients, tend to be more liberally assessed, only because their application is better (but only partly) understood by most doctors. Once again, little knowledge is dangerous, and worse than no knowledge. Humility and no knowledge often co-exist, and are by enlarge harmless. It is the association of little knowledge and pride which remains the dangerous intellectual posture. Enough of the carping...

TABLE 1

NEW TRENDS WITH SINGLE PHOTON LABELS

^{99m}Tc	: considerable progress but fundamental research still needed to understand basic chemistry. Advances with cationic complexes.
^{123}I	: important future. Main problem remains cost/mCi
^{97}Rt	: very interesting chemistry entirely to be explored

NEW TRENDS WITH SINGLE PHOTON LABELS (II)

ANTIBODY	FATTY ACIDS
LIPOSOME	COLLOIDS
RECEPTOR LIGAND	ADRENERGIC BLOCK
pH GRADIENT	CELL LABELLING
BI FUNCTIONAL CHELATE	THROMBUS DEPOSITION

Why is Nuclear Medicine such an exciting subject? Let us be reminded by Claude Bernard's assessment: «Claude Bernard me disait un jour "Nous saurons la physiologie lorsque nous pourons suivre pas à pas une molécule de carbone ou d'azote, faire son histoire, raconter son voyage dans le corps d'un chien, depuis son entrée jusqu'à sa sortie". (Taine, H.A. (1981). Histoire de la France, Vol. 7, p. 28».

There is no better description of what Nuclear Medicine is about! Indeed, it is only with the radioactive tracer method that the above can and is being achieved. We have the tools, the methodologies, the models and the main areas for fundamental research. Cyclotrons, positron emitting radionuclides, positron detection instrumentation and computers are some of the tools at our disposal. The models permit the measurement of absolute values of blood flow in ml/min/gr, of oxygen utilisation in ml of O_2 consumed per ml of tissue per minute, of glucose utilisation, palmitate utilisation, of protein synthesis via ^{11}C-methionine, and so on. Absolute concentration of drugs in man can be investigated, in normal and pathological tissue. Of course this methodology is costly, time consuming, labour and know-how intensive and will only bear fruit in highly organised and developed medical institutions. But the data is emerging and Claude Bernard's vision is being pieced together.

TABLE 2 NEWER RADIOPHARMACEUTICALS

Mechanisms of Localization and Tracers		Target Organs and Applications
pH Gradient:	PIPSE and MOSE (at present ^{75}Se)	Brain and heart
Antibodies:	CEA, AFP, HCG + others (^{131}I)	Tumours
Liposomes:	progress with negative charge	Cell Membrane and Drug Transport
Receptor Ligands:	iodophenylalkyl amines (^{123}I)	Brain, Retina and Neural Tumour
	meta iodo benzyl guanidine (^{123}I)	Adrenal Medulla, Heart
	alfa-methyl-tyrosine (^{123}I)	Pheocromocitoma Melanoma
	N-isopropyl-p-(^{123}I)-iodoamphetamine	Brain Blood flow
Metabolic Analogs:	fatty acids(^{123}I) ω-iodo hexadecanoic ω-iodo heptadecanoic	Heart
Oestrogen Receptor:	1 - fluoro $^{3}H_4$ Hexestrol (^{123}I)	Breast, Prostate, Adrenal Cortex
	0 - fluoro $^{3}H_3$ Hexestrol	
	17 beta - 16 alfa- Iodoestradiol	
Diffusable Tracer	Antipyrine (^{123}I)	Brain, Lung
Bifunctional Chelates	$^{99m}TcO_2$ (DIARS) $_2Br_2$	Heart
	^{99m}Tc- Lidocaine Deriv.	Liver + Bile
Cell Labelling	^{111}In-Leucocytes, Platelets	Abcess Thrombus

Nuclear Medicine is however far more than a powerful research tool. It is a well established *medical speciality*, offering a wide range of diagnostic and therapeutic routines. Once again, the fundamental advantage of Nuclear Medicine lies in its ability to routinely expand on its available radiopharmaceuticals for tracer work. Whilst Table 1 and Table 2 highlight the main areas of development of new tracers labelled with conventional radionuclides such as ^{99m}TC, ^{123}I, ^{131}I, ^{111}In, etc (and an impressive list it is, even on a superficial analysis alone), a number of specific examples can be given, where clinical Nuclear Medicine is expanding.

In the important area of cell labelling, it is now possible to label whole blood elements or well identified groups. Red cells, white cells, neutrophils, lymphocytes, platelets, they can all be labelled and successfully applied to the clinical problem. Techniques have therefore emerged to detect and localise acute bleeding of the gastrointestinal tract, to investigate localisation and formation of platelet aggregation in post surgical or catheter procedures, to demonstrate and monitor sites of suspected infection, to evaluate the activity of Crohn's disease and ulcerative colitis, etc. New hepatobiliary compounds and labelled bile acids allow for the evaluation and differential diagnosis of the acute abdomen, the study of small and large bowel disease and the investigation of malabsorption syndromes, the demonstration of bile flow in pre and post surgical conditions and the establishment of the presence and magnitude of biliary reflux.

New metabolic analogues are chanching traditional techniques of investigation. Brain scintigraphy is witnessing a rebirth via ^{123}I labelled amines and the measurement of regional cerebral blood flow is increasingly in demand in the assessment of TIA and its management. For the first time we are able to visualise and more significantly localise areas of focal epilepsy, pinpointing to the neurologist and neurosurgeon areas of abnormality, even when silent on rest and stress EEG methodology. ^{131}I labelled meta-iodobenzyl-guanidine represents a major breakthrough, not only in the diagnosis of pheocromocytoma but also in its treatment. At last, and after iodide, we seem to have a second *magic bullet* for investigative and therapeutic purposes. Finally and just to mention an entirely new approach, let us underline the fundamental advance being achieved with the large scale production of monoclonal antibodies and the hibridoma technique. Tumour associated antibodies are being produced and labelled with radionuclides and the imaging of malignancy is being looked at with a new perspective. FAB II fragments have been labelled with ^{99m}Tc, without significant loss of their basic reactive properties.

Nuclear Medicine, as a branch of medicine, is alive and kicking in many fascinating directions. *Provided it is practised by appropriately trained doctors* supported by adequate technical services and personnel, it is an indispensable area of activity for any moderate to major hospital environment.

Peter Josef Ell

Institute of Nuclear Medicine
Middlesex Hospital Medical School
Mortimer Street
London W1 8AA. U.K.