《招待講演 (1)》

Contribution of Radionuclide Studies to Pulmonary Medicine and Physiology

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PAST

The first pulmonary radionuclide studies were carried out by Knipping (1955) in Germany using inhaled ^{131}I-methyl iodide vapour, measuring regional ventilation and blood flow in patients with lung cancer. This early work was followed by studies at Hammersmith Hospital (1958–1962) using short-lived positron emitters such as ^{15}O ($t\frac{1}{2}$ 2.1 min) in the form $C^{15}O_2$ or $C^{15}O$ by West, Dollery and Hugh-Jones (1963). Regional $\dot{V}$, $\dot{Q}$ and diffusion were measured and systematic vertical gradients, determined by gravity, described. Positrons can only be used in the vicinity of cyclotrons and the reactor-produced radioactive gas (^{133}Xe) with a 5.3 day half-life was more convenient.

In the 1960's Physiological studies in Montreal and London, using ^{133}Xe for $\dot{V}$ and $\dot{Q}$ distribution, described the pattern of regional expansion in the lung [the Milic-Emili (1966) onion-skin diagram] and analysed the distribution of pulmonary blood flow in terms of the relationships between pulmonary arterial, venous and alveolar pressures (Zones I, II and III); later Zone IV was added (Hughes et al, 1988).

Radioactive gases are not a practical means for routine measurements of pulmonary blood flow. An important advance was the technique of intravenous injection of ^{99m}Tc-labelled albumin macroaggregates or microspheres (10–40 μm diameter) which measured $\dot{Q}$ distribution by impaction in small pulmonary vessels [Wagner et al, and Taplin et al (1964)]. The replacement of individual scintillation detectors by the Anger gamma camera made whole lung imaging possible and the detection of pulmonary emboli (or, just as important, the exclusion of that diagnosis) feasible. This was the first major impact of radionuclides on the practice of pulmonary medicine. On the other side of the alveolar capillary membrane, radiolabelled aerosols were introduced. Insoluble aerosols (^{99m}Tc-labelled albumin particles 4–10 μm diameter) were used to image mucociliary clearance (Camner, 1980; Pavia et al, 1980). Soluble aerosols such as ^{99m}Tc-DTPA (c. 1 μm particle size) measured alveolar-capillary transfer, chiefly diffusion across the alveolar epithelium (Jones et al, 1983; Chopra et al, 1978). Krypton-81m gas ($t\frac{1}{2}$ 13 sec) was introduced as a simple and convenient radionuclide for imaging regional ventilation (Fazio and Jones, 1975). Radiolabelled aerosols are an alternative method.

PRESENT

In the 1980's, radionuclide studies have extended their range considerably and there have been exciting advances in technology and radiochemistry. Lung injury can be assessed with inhaled ^{99m}Tc-DTPA or with i.v. ^{113m}In-transferrin. Cell labelling e.g. ^{113m}In-neutrophils, can assess the distribution and extent of pulmonary inflammation. Metabolic compounds (^{18}F-deoxyglucose) (Nolop et al, 1987), pharmacological (^{11}C-Ketanserin) (S2 antagonist) (Syrota, 1987) and enzymatic (^{11}C-acetazolamide) ligands, and amine-related compounds (^{123}I-iodobenzyl propanediamine, ^{11}C-imipramine, ^{11}C-propranolol) are being investigated. The uptake of drugs (^{11}C-erythromycin) into pulmonary tissues (i.e. in pneumonia) has been investigated using PET (Wollmer et al, 1982) Tomography [single photon emission computerized tomography (SPECT) (Orphanidou et al, 1986) or positron emission

tomography (PET) (Hughes 1985, 1987)] is a notable technical advance.

FUTURE

It is likely that diagnostic imaging will focus on individual cell types or molecules using monoclonal antibodies (for neoplastic cells, platelets, endothelial and epithelial surfaces). In addition, radioligands will be developed for surface receptors and cell markers (adrenergic and muscarinic receptors, epidermal growth factor, EDRF etc).

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《招待講演 (2)》

Two Decades of Research on Adrenal Imaging Agents

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Our research on adrenal imaging agents began in the mid 1960's. Although this work led to imaging agents for both adrenalcortical and medullary tissue, the focus of this presentation will be on the former. Our approach to the design of such radiopharmaceuticals has involved rationales based upon known pharmacology of drugs (e.g. o,p'-DDD) and biochemistry of hormones (e.g. steroids). The initial studies with radioiodinated steroids turned out to be the most promising and led to the development of ^{131}I-19-iodocholesterol as the first successful adrenal imaging agent. Several years later Kojima and coworkers described the isolation of a rearranged product of ^{131}I-19-iodocholesterol and found it to be ^{131}I-6β-iodomethyl-norcholest-5(10)-en-3β-ol; a product which turned out to be clinically superior to ^{131}I-19-iodocholesterol. During this time our own studies centered on determining the mechanism for the selective accumulation of ^{131}I-19-iodocholesterol in steroid-secreting tissues and tumors. We found that when 19-radioiodinated cholesterol was administered to female rats, over 85% of the radioactivity present in the adrenals and ovaries