complete occlusion. Repeated generation of Phase 1 in isolation (every 5 s for 5 min) produced a marked but incomplete tachyphlaxis. When this was followed immediately by stimulation for 30 s, to generate the full biphasic response, phase 2 was also found to have been substantially reduced in magnitude. Thus stimulus parameters which generate only phase 1 also activate and fatigue the mechanisms responsible for phase 2.

Experiments were performed in which different portions of the vas were perfused and stimulated. Phase 1 of the response was generated by all portions but Phase 2 was absent from the quarter of the vas at the prostatic end.

Phase 1 of the response was more resistant than phase 2 to guanethidine, but at 1×10^{-4} M both were blocked.

It is therefore suggested that both phases of the response are mediated by noradrenergic nerves. The preparation and results referred to above will be demonstrated.

References

FASTIER, F.N. & SMIRK, R.H. (1947). Circulatory properties of iso-thioureas, guanidines, iso-ureas and amidines. *J. Pharmac. exp. Therap.*, **89**, 256–270.

JACKSON, A.R., SHORT, A.H. & TOMLINSON, D.R. (1978). A flow-sensitive apparatus for studying the responses of the constrictor muscles of perfused tubular organs. *J. Physiol. Lond.*, **276**, 13–14P.

The use of gamma cameras to measure the disposition and fate of iodide in the rabbit

J.G. HARDY[1], MICHELE LEESON[1] & C.G. WILSON[2] (introduced by T. BENNETT)

[1]*Department of Medical Physics and* [2]*Department of Physiology and Pharmacology, Medical School, Queen's Medical Centre, Clifton Boulevard, Nottingham NG7 2UH*

The use of gamma cameras to follow the distribution of γ-emitting radiopharmaceuticals as a diagnostic aid in patient management has been well documented (Craddock & MacIntrye, 1977). We have now used the gamma camera to follow the distribution of [^{131}I]-sodium iodide, since we wish to use this nuclide as a marker of novel drug formulations.

Seven rabbits received, by intravenous administration, 0.2 ml of sodium iodide solution (100 picomoles) containing 100 μCi of ^{131}I in isotonic saline. For the ensuing 200 h anterior images of the rabbit were recorded at intervals using a Searle LFOV gamma camera linked to a Varian V76 data processor. Regions of interest were defined over the neck, stomach, urinary bladder and thigh muscle; and the radioactivity within these regions was quantified. The data obtained were corrected for radioactive decay and for background activity. The results are shown in Table 1. Whole body elimination of iodide was

Table 1 Whole body elimination of ^{131}I-sodium iodide and distribution to bladder, stomach and neck with time. Means (± s.e. mean) derived from seven rabbits

	% *Administered dose remaining with time (h)* *Region of interest*			
Time (h)	*Whole body*	*Neck*	*Stomach*	*Bladder*
0	100 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
2	102.54 ± 2.22	1.08 ± 0.29	2.48 ± 0.53	1.77 ± 0.68
5	93.35 ± 4.33	0.93 ± 0.26	2.52 ± 0.74	7.02 ± 1.77
10	80.93 ± 3.35	1.71 ± 0.51	3.10 ± 0.84	10.16 ± 3.47
15	60.71 ± 5.90	2.53 ± 0.60	3.14 ± 0.72	4.53 ± 1.28
20	50.21 ± 7.16	2.80 ± 0.78	2.59 ± 0.81	2.42 ± 0.76
25	41.44 ± 8.67	3.04 ± 0.54	2.10 ± 0.60	1.62 ± 0.83
30	34.87 ± 7.54	3.03 ± 0.52	1.82 ± 0.91	3.38 ± 0.49
40	29.15 ± 6.91	3.42 ± 0.68	0.82 ± 0.34	3.28 ± 1.20
50	22.50 ± 6.92	3.71 ± 0.73	0.66 ± 0.35	1.49 ± 0.64
60	17.86 ± 6.46	4.06 ± 0.78	0.24 ± 0.14	1.14 ± 0.76
80	14.14 ± 5.66	4.09 ± 0.72	0.32 ± 0.31	0.47 ± 0.35
100	12.20 ± 4.85	4.23 ± 0.88	0.10 ± 0.10	0.03 ± 0.03
150	9.21 ± 3.41	3.86 ± 0.69	0.09 ± 0.09	0.05 ± 0.05
200	7.10 ± 2.40	3.59 ± 0.67	0.15 ± 0.13	0.03 ± 0.02

found to follow multiexponential kinetics; 50% of the dose was eliminated within 20 h and 90% by 130 h, the majority of the tracer being concentrated in the neck region at the latter time.

The highest amount of radioactivity was found in the bladder at 10 h, with a lesser peak at about 35 hours. Uptake of iodide by the stomach reached a peak at 15 h and then declined with a $T_{1/2}$ of 14 hours. The thyroid gland showed a gradual uptake of iodide reaching a maximum of 4% of the dose by 10 h followed by a slow elimination over the remainder of the study.

At the end of 200 h 6 of the 7 rabbits were killed, the thyroid glands removed and the radioactivity due to ^{131}I was measured. These measurements suggested that the levels of radioactivity found in the neck region were largely due to uptake of ^{131}I by the thyroid gland. The maximum uptake of iodide by the rabbit thyroid was found to be lower than the literature value of thyroid ^{131}I-uptake in man (Berman, Braverman, Burke, De Groot, McCormack, Oddie, Rohrer, Wellman & Smith, 1975).

References

BERMAN, M., BRAVERMAN, L.E., BURKE, J., DE GROOT, L., McCORMACK, K.R., ODDIE, T.H., ROHRER, R.H., WELLMAN, H.N. & SMITH, E.M. (1975). Summary of current radiation dose estimates to humans from ^{123}I, ^{124}I, ^{125}I, ^{126}I, ^{130}I, ^{131}I and ^{132}I as sodium iodide. *J. Nucl. Med.*, **16**, 857–860.

CRADDOCK, T.D. & MACINTRYE, W.J. (1977). Camera-computer systems for rapid dynamic imaging studies. *Seminars in Nuclear Medicine*, **7**, 323–336.

A technique for measuring first pass extraction in the rat perfused liver

J.O. IBU, I.A. MACDONALD
& A.H. SHORT
(introduced by T. BENNETT)

Department of Physiology and Pharmacology, Medical School, Queen's Medical Centre, Clifton Boulevard, Nottingham NG7 2UH

A technique for studying the hepatic first pass extraction of compounds of physiological and pharmacological interest is described. The liver is perfused *in situ* using the technique of Hems, Ross, Berry & Krebs (1966). Following cannulation, the liver is perfused in a closed-circuit, constant pressure system for an initial 30 min stabilisation period, and also between each experimental run.

The experimental runs are performed in the following way. A solution is prepared which contains 0.5 μCi of the radioactively labelled [^{3}H] or [^{14}C] test substance and 0.5 μCi of the labelled [^{14}C] or [^{3}H] intravascular or extracellular reference substance in 1 ml of perfusate. The perfusion system is then switched to open-circuit and the radioactive mixture is infused into the perfusion line, close to the portal vein cannula, at a rate of 0.4 ml/min for 40 seconds. At the same time the hepatic venous effluent is collected in sample vials at 1.5 s intervals (using an automatic sample changer (Hook & Tucker, A40)) for up to 60 seconds. Aliquots of the infusion mixture and each venous effluent sample are then deproteinised in perchloric acid (8% w/v) and prepared for liquid scintillation counting as described by Hooper & Short (1977). The hepatic extraction of the test substance under consideration is then calculated from a knowledge of the d/min of the test and reference substance in the infusion mixture and in the hepatic venous effluent (Hooper & Short, 1977). The results of a typical experiment are presented in Figure 1 where the ratio test d/min/reference d/min in the infusate and the samples are then used to calculate the extraction.

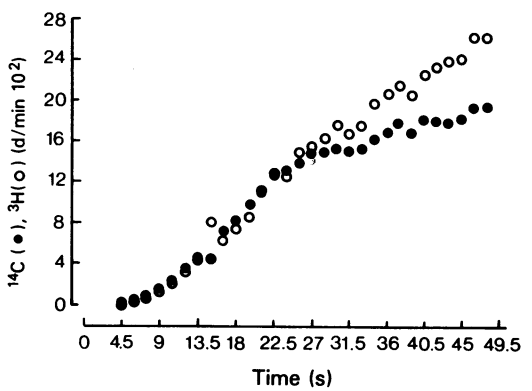

Figure 1 Showing levels of radioactivity of reference ([^{14}C]-L-Glucose) and test ([^{3}H]-D-Glucose) substances in hepatic venous samples during a 40 s infusion. (Infusion mixture [^{3}H]: [^{14}C] d/min ratio = 1.70).

We are grateful to Ahmadu Bello University Zaria, Nigeria for the grant (Study Fellowship) to one of us (J.O.I.) in support of this work.

References

HEMS, R., ROSS, B.D., BERRY, M.N. & KREBS, H.A. (1966). Gluconeogenesis in the perfused rat liver. *Biochem. J.*, **101**, 284–292.

HOOPER, R.H. & SHORT, A.H. (1977). Hepatocellular uptake of glucose, galactose and fructose in conscious sheep. *J. Physiol. Lond.*, **264**, 523–539.