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### A computer model simulating human glucose absorption and metabolism in health and metabolic disease states

A computer model designed to simulate integrated glucose-dependent changes in splanchnic blood flow with small intestinal glucose absorption, hormonal and incretin circulation and hepatic and systemic metabolism in health and metabolic diseases e.g., non-alcoholic fatty liver disease, (NAFLD), non-alcoholic steatohepatitis, (NASH) and type 2 diabetes mellitus, (T2DM) demonstrates how when glucagon-like peptide-1, (GLP-1) is synchronously released into the splanchnic blood during intestinal glucose absorption, it stimulates superior mesenteric arterial (SMA) blood flow and by increasing passive intestinal glucose absorption, harmonizes absorption with its distribution and metabolism. GLP-1 also synergizes insulin-dependent net hepatic glucose uptake (NHGU). When GLP-1 secretion is deficient post-prandial SMA blood flow is not increased and as NHGU is also reduced, hyperglycemia follows. Portal venous glucose concentration is also raised, thereby retarding the passive component of intestinal glucose absorption. Two NASH-related mechanical defects; increased pre-hepatic sinusoidal resistance combined with portal hypertension open intrahepatic portosystemic collateral vessels. The model reveals the latent contribution of portosystemic shunting in development of metabolic disease. This diverts splanchnic blood content away from the hepatic sinuses to the systemic circulation, particularly during the glucose absorptive phase of digestion, resulting in inappropriate increases in insulin-dependent systemic glucose metabolism. This hastens onset of hypoglycemia and thence hyperglucagonemia. The model reveals that low rates of GLP-1 secretion, frequently associated with T2DM and NASH, may be also be caused by splanchnic hypoglycemia, rather than to intrinsic loss of incretin secretory capacity. These findings may have therapeutic implications on GLP-1 agonists or glucagon antagonist usage.

### Biography

Richard J Naftalin graduated in medicine from Glasgow University. Following completion of medical registration at Glasgow Royal Infirmary studied at University College London for an M Sc in Biochemistry and then at the National Institute for Medical Research Mill Hill, for a Ph D in Biochemistry. Joined the Physiology dept at Leicester University in 1968 as a lecturer and after seven years moved to King's College London Dept of Physiology as Senior Lecturer, appointed as Professor in Physiology 1990.

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