

First 2011
VIVA 6

Describe the physiology of Insulin This viva began with a discussion on the physiology of insulin, physiological consequences of insulin deficiency, oral hypoglycaemic drugs and the thyroid gland. Generally candidates performed well in this viva. The role of insulin beyond metabolism of glucose, fat and protein was not well understood. The differences in the pharmacology between T4 and T3 was another area of weakness.

“Describe the physiology of insulin”

insulin is a polypeptide which consists of two chains of amino acids linked by dipeptide bonds
it is secreted from the beta cells of the islet of langerhans in the pancreas in response to raised BSL
its mechanism of action is anabolic, increasing glucose entry into cells, protien, fat and glycogen prod
it inhibits catabolic process such as lipid and protien breakdown
it causes increased potassium entry into cells
along with glucagon is the main regulator of glucose homeostasis
it is destroyed by proteases and its half life in the circulation is about 5 minutes

“What are the consequences of insulin deficiency?”

decreased entry of glucose into the cells, impaired energy production
increase in catabolic processes, glycogenolysis and gluconeogenesis with lipid and protien breakdown
high BSL overwhelms the kidney's ability to reabsorb glucose, osmotic diuresis and glycosuria develops
the products of lipid and protien breakdown accumulate leading to a ketoacidosis (via Acteyl-CoA)
buffering occurs increasing acid production with a decrease in HCO₃, and hyperventilation to drop CO₂
as a result of the metabolic acidosis sodium and potassium are depleted
eventually the patient is overwhelmed, coma, decreased ventilation and death results

“Discuss the mechansim of several hypoglycaemic agents”

Sulphonylureas - glicazide

displace insulin from beta cells, increase beta cell production and reduce peripheral resistance
may precipitate hypoglycaemia therefore caution in elderly, or pts with heart disease
high bioavailability, metabolised via CYP450 enzymes, halflife 10 hrs, excreted urine inactive met

Biguanides - metformin

delayed gut uptake of glucose, increased peripheral sensitivty, inhibits gluconeogenesis
muscle cramping and pain in 10% pts, lactic acidosis in renal impairment and etoh abusers
slow absorption, bioavail 60%, duration several days, v.large vd, not metab, excreted unchanged

Glitazones - rosiglitazone

reduce the resistance of peripheral tissues to insulin
can cause fluid retention and should be avoided in pts with heart failure
v.high bioavail ~100%, delayed onset of action, metab liver CYP450, HL 4hrs, urine inactive met

“What is the significance of thyroid hormone”

it is important for growth and development, the regulation of intermediary metabolism, and has effects on the cardiovascular system

“What is the significance of T3 and T4?”

there is a feedback loop between the hypothalamus (TRH), ant pituitary (TSH) and thyroid (T4 and T3)
thyroxine is also known as T4 and tri-iodothyronine is also known as T3
T3 and T4 are the tyrosine based hormones released from the thyroid gland, T3 is x3-4 as potent as T4
T4 can be converted peripherally into the far more active T3 or the inactive rT3 in starvation states
Most thyroxine in plasma is bound to thyroxine binding globulin 70%, albumin 20%, prealbumin 10%
Only very small amounts exists as the physiologically active free T3 0.3 and free T4 0.03