CHEMICAL PATHOLOGY ASSIGNMENT

QUESTION 1

A 45 year old woman presented with complaints of irritability, depression and hot flushes. Her periods had become irregular over the past 6 months. She had been on treatment for hypertension with a beta-blocker and an ACE inhibitor for 6 years.

i. What is the most likely explanation for her symptoms? Menopause ↓ Progesteron
ii. What tests can be used to confirm this? Blood Oestrogen + Progesteron levels
iii. What do the results indicate? ↑FSH + ↓P.
iv. What treatment options can be offered to control her symptoms? Hormone Replacement Therapy.
v. Besides alleviating the symptoms, what additional benefits does HRT confer?
- Maintains the Endometrium
- Prevents Osteoporosis

QUESTION 2

A 20-year old man presented with pubertal delay. On examination he was of normal height and had a eunuchoid body shape. Pubic and axillary hair was sparse, the genitalia were prepubertal, and both testes were present in the scrotum. Plasma testosterone: 3.0nmol/L (N 8.4-30), LH: 0.3 U/L (N 0.4 - 5.5), FSH: 1.2 U/L (N 0 - 16)

i. Define the meaning of the terms primary hypogonadism and secondary hypogonadism. Primary caused by lack of
ii. What type of hypogonadism is present in this patient? (i.e. at what level is the lesion?)
iii. Suggest some possible causes of male primary (hypergonadotropic) hypogonadism.
iv. Suggest some possible causes of male secondary (hypogonadotropic) hypogonadism.
v. Questioning of the patient revealed that he had no sense of smell, and had never had one.
vi. Does the finding of anosmia have any special significance in this context?

QUESTION 3

A one-month old girl was investigated for ambiguous genitalia. The pregnancy and birth had been normal, and the baby had gained weight normally and had shown no signs of illness. Ambiguous genitalia were noted at birth. The clitoris was enlarged and there was partial fusion of the labia. An ultrasound scan showed the presence of a uterus. An XX karyotype was found in peripheral blood. Biochemical tests on plasma revealed the following (reference intervals in brackets): Na+ : 135mmol/L, K+ : 4.3mmol//L Cortisol (11 am): 313nmol/L (9 am: 140-700), (11 pm: 0-138) Testosterone: 6.6nmol/L (<1 prpubertal) (8.4-30 adult male) (<2.7 adult female), 17-OH-progesterone: 356nmol/L (<6), Androstenedione: 19.4 nmol/L (<12)

i. What is the diagnosis
ii. Explain the reason for the overproduction of androgens
iii. Would you expect the levels of plasma ACTH to be elevated, decreased or normal?
iv. Comment on the cortisol level.
v. Is it necessary to treat this condition? Why?
vi. Explain the principles of therapy in this disorder.
vii. What are the genetics of the condition? And what advice would you give the parents regarding future children?

(note: after 4 weeks of hydrocortisone therapy the following labs were obtained: 17-OH-progesterone: 14nmol/L, Testosterone: 1.2nmol/L)

QUESTION 4

A 3 week old boy was admitted for investigation of his failure to gain weight. There was no history of diarrhoea or vomiting, and examination revealed nothing of diagnostic significance. On the third day of admission the baby became clinically dehydrated. Biochemical tests on plasma revealed the following: Na+ 106 mmol/L, K+ 6.2 mmol/L, Cl80 mmol/L, HCO3 14 mmol/L, Urea 6.5 mmol/L, mol/L, Glucose 4.5 mmol/LμCreatinine 50

i. Calculate the plasma osmolality and anion gap.

ii. What type of acid-base disturbance is present?

iii. Suggest one or more possible diagnoses.

Further blood and urine samples were taken for endocrine investigations. Treatment comprising IV saline, glucocorticoid (cortisone acetate) and mineralocorticoid (fluorocortisone) was commenced. Plasma electrolytes, osmolality and hydration state

normalized over the next 9 days. Results of endocrine investigations were as follows: Plasma 17-OH-progesterone 2240 nmol/L (N<6)

iv. What is your final diagnosis
v. Would you expect the plasma renin level to be low, normal or high?
vi. Which adrenal enzyme deficiency presents with hypertension? (Give the mechanism)

QUESTION 5

A 19 year old woman presented with primary amenorrhoea. She was normal in appearance, except for the almost complete absence of pubic and axillary hair. Gynaecological examination revealed a short, blind-ended vagina, and no cervix was palpable. Radiology showed absence of the uterus. Blood karyotyping showed XY chromosomes. Plasma testosterone 29nmol/L (adult female 1-2.8; adult male 8.4-30). The diagnosis is that of androgen insensitivity syndrome. This is due to a defect in the androgen receptor, leading to androgen resistance, complete in this case. Other mutations cause incomplete androgen resistance, giving rise to a spectrum of genital abnormalities ranging from hypospadias to completely female external phenotype. All are X-linked, since the androgen receptor gene is located on the X chromosome. The testes are inguinal or abdominal. The essential biochemical feature is a high level of testosterone in the presence of incomplete masculinisation. Adrenal androgen precursors are not elevated as seen in CAH.

i. Why is there an absence of internal genital organs in this disorder?

ii. What is the inheritance pattern and typical family history of androgen insensitivity syndrome?

iii. List the 3 zones of the adrenal cortex and the hormones produced there.

iv. What is meant by the terms (a) adrenarche (b) thelarche (c) menarche?

v. Which structures are derived from (a) the Wolffian ducts (b) the Mullerian ducts? How is the fate of these primitive structures determined?

vi. What is meant by “hypospadias” and “cryptorchidism”?

Question one