1(a). Ageing is known to affect the male urinogenital system in a number of ways.

Fig. 35.1 is a diagram of the male urinogenital system.

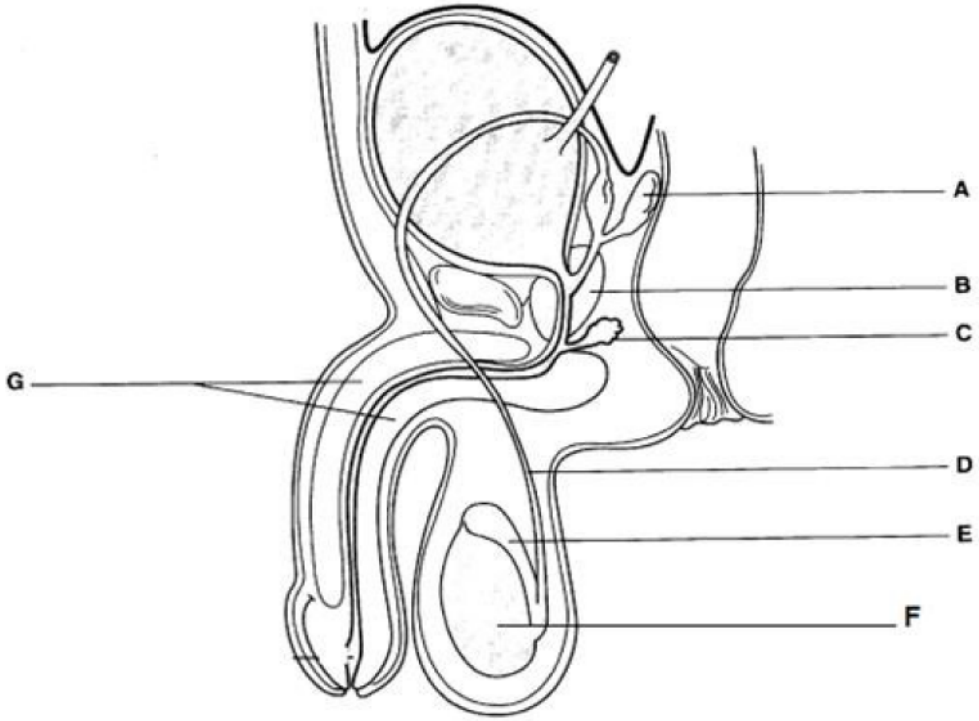

Fig. 35.1

Complete Table 35.1 below so that the correct letter from Fig. 35.1 is against each of the following statements:

Statement	Letter
If this is enlarged it can lead to difficulty in starting to urinate or emptying a full bladder.	
Changes in this structure mean sperm can fail to become motile.	
Changes in this structure can lead to more chromosome abnormalities in sperm.	
Changes in tissues here can lead to erectile dysfunction.	

Table 35.1

[4]

(b). Cyclic **AMP** acts as an intracellular messenger molecule in many cells.

The sequence of cellular events which happens in a normal erection is described below:

- stimulation of tissue causes the release of a cell signalling molecule (nitrogen monoxide) from nerve endings
- nitrogen monoxide diffuses into neighbouring cells and causes the production of an intracellular messenger molecule, cyclic **GMP**
- cyclic GMP causes smooth muscle in cells in blood vessel walls to relax
- cyclic GMP is then broken down by an enzyme **PDE-5**.

(i) Comment on the properties of nitrogen monoxide as a cell signalling molecule.

---

[2]

(ii) The chemical sildenafil citrate (Viagra®) binds to the active site of the enzyme **PDE-5**.

Suggest how the action of Viagra® makes it an effective treatment for erectile dysfunction.

---

[3]

2. The process of ageing produces changes in many body systems. One effect of ageing on the reproductive system in women is the onset of the menopause.

Discuss the risks **and** benefits of the options available to women for **treating** symptoms of the menopause.

[8]

3. The World Health Organisation collects data on the global distribution of many diseases including **osteoarthritis**. The statistics that are calculated are used in a range of epidemiological studies.

One important statistic that can be calculated is the disability-adjusted life year or **DALY**.

- One DALY can be considered as one lost year of **healthy** life.
- In North America the DALY for osteoarthritis is 796 000.
- In Africa the DALY for osteoarthritis is 650 000.

Another important statistic that can be calculated is life expectancy at birth.

- In North America life expectancy is 74.
- In Africa life expectancy is 50.

Both sets of statistics are based on data collected in the year 2000 and are for both males and females.

(i) How does the statistical evidence support the conclusion that the onset of osteoarthritis in Africa happens at an earlier age?

---

[2]

(ii) Suggest why the onset of osteoarthritis happens at an earlier age in Africa.

---

[2]

(iii) The data used for calculating the DALYs for osteoarthritis were combined data from males and females.

Explain why it would **not** be appropriate to combine male and female data for epidemiological studies on **osteoporosis**.

[2]

4. Symptoms of the menopause such as hot flushes can be treated by hormone replacement therapy (HRT).

Some forms of HRT are provided as implants.

Explain why cyclical HRT treatments are not available as implants.

[1]

5(a). The age at which a woman goes through the menopause depends on several factors.

- Smoking, unemployment and being at higher risk of coronary heart disease are factors linkedto a lower age of menopause.
- Having children, use of oral contraception and having a lower BMI are factors linked to a higher age of menopause.
- The age of menopause varies between different ethnic groups.

In a study involving large populations of women, the median age of 'natural menopause' in a population was found to be 50.4 years.

(i) Suggest what is meant by natural menopause.

---

[2]

(ii) A **median** value for a large population is obtained as follows:

- all the values obtained are placed in order from lowest to highest
- the median is the middle value in the range.

Suggest why the **mean** age of menopause can vary significantly between populations but the **median** does not.

---

[2]

(b). Chemicals in cigarette smoke have been shown to cause damage to cells in ovaries. Damaged cells are no longer able to perform their normal function.

Explain how damage to cells in the ovaries could result in an earlier onset of the menopause.

[2]

6.

Fig. 2.2 shows how the number of ovarian follicles changes from birth to 50 years of age.

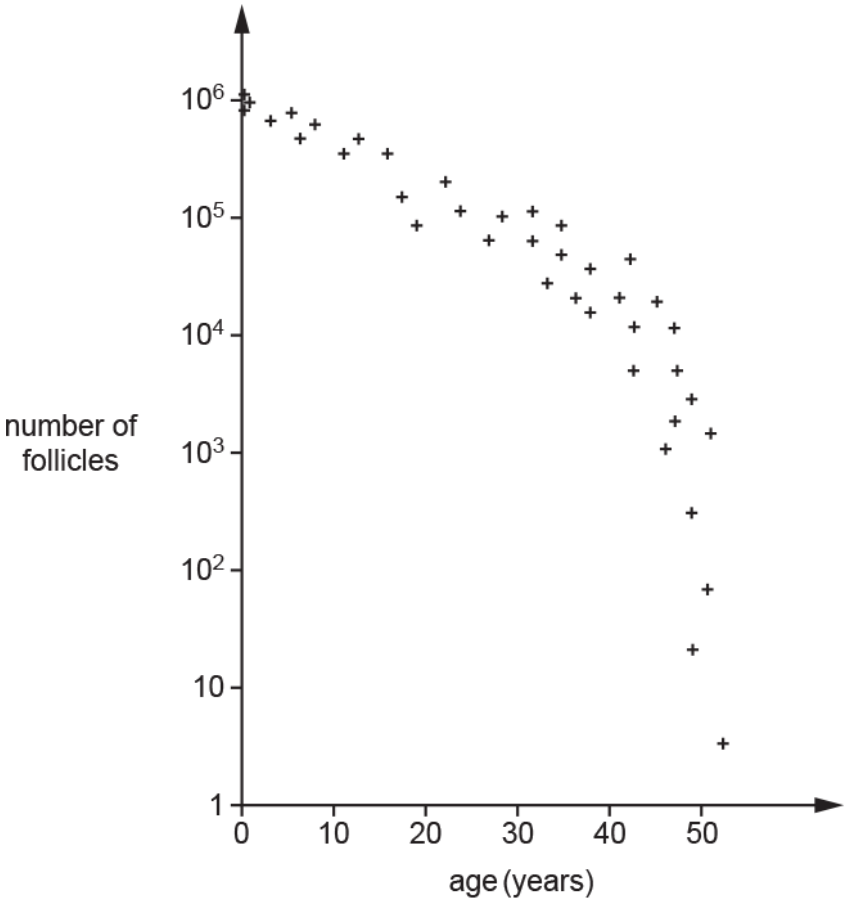

Fig. 2.2

(i) Using the data in Fig. 2.2, describe **and** explain the relationship between the number of follicles and age.

---

[4]

(ii) Name the biological process that occurs as a result of changes in the number of follicles between 45 and 50 years of age.

---

[1]

(iii) Describe **two** symptoms that women may experience during this process

---

---

[1]

7(a).

Physiological ageing leads to changes in the male reproductive system. These changes can cause infertility and erectile dysfunction.

(i) Explain the difference between male infertility and erectile dysfunction.

---

[2]

(ii) State one factor, other than physiological ageing, that can cause erectile dysfunction.

---

[1]

(b). Hormone replacement therapy (HRT) is used to treat the symptoms of the menopause in some women. However, the molecules used in HRT can cause side effects.

Fig. 4 shows the results of a study, published in 2002, of the effect of HRT on the incidence of various conditions.

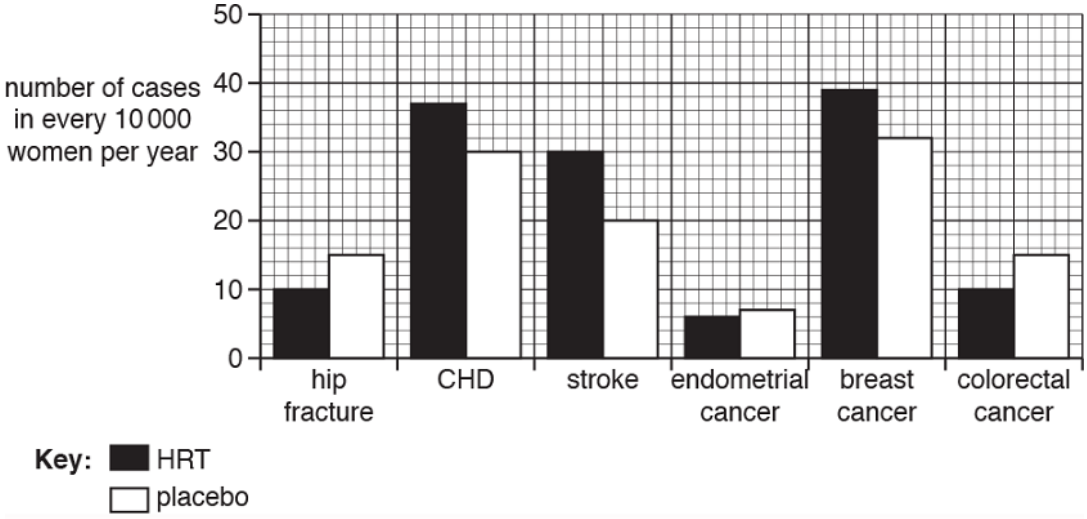

Fig. 4

(i) Use Fig. 4 to assess the effect of HRT on the incidence of disease and injury.

[3]

(ii) * In November 2015 the National Institute for Health and Care Excellence (NICE) issued new guidelines for managing the menopause. These included:

- Women with cardiovascular risk factors should not automatically be excluded from taking HRT.
- Oestrogen-only HRT causes little or no increase in the incidence of breast cancer; HRT with oestrogen and progesterone can increase incidence of breast cancer, but any increased risk reduces after stopping HRT.

Use your own knowledge and these new guidelines to evaluate the risks of HRT.

[6]

END OF QUESTION PAPER

<table>
<tr><th colspan="3">Question</th><th>Answer/Indicative content</th><th>Marks</th><th>Guidance</th></tr>
<tr><td>1</td><td>a</td><td></td><td>
<table>
<tr><th>Statement</th><th>Letter(s)</th></tr>
<tr><td>If this is enlarged it can lead to difficulty in starting to urinate or emptying a full bladder.</td><td>B</td></tr>
<tr><td>Changes in this structure mean sperm can fail to become motile.</td><td>E</td></tr>
<tr><td>Changes in this structure can lead to chromosome abnormalities in sperm.</td><td>F</td></tr>
<tr><td>Changes in tissues here can lead to erectile dysfunction.</td><td>G</td></tr>
</table>
</td><td>4</td><td></td></tr>
<tr><td></td><td>b</td><td>i</td><td>Any 2 from:
idea that nitrogen monoxide must be, lipid soluble / hydrophobic
(explanation) it diffuses / AW, through the cell surface membrane
binds to, receptor / AW, inside the cell
idea that second messenger is cyclic GMP rather than cyclic AMP</td><td>2</td><td></td></tr>
<tr><td></td><td></td><td>ii</td><td>Any 3 from:
Viagra acts as a competitive inhibitor (of PDE-5)

idea that cyclic GMP, is not broken down / lasts longer (in cells)
idea that blood vessels dilate, more / for longer
idea that erection maintained for longer</td><td>3</td><td>ALLOW ‘Viagra forms an enzyme inhibitor complex’ OR description ‘prevents the formation of ESC’</td></tr>
<tr><td></td><td></td><td></td><td>Total</td><td>9</td><td></td></tr>
</table>

Question			Answer/Indicative content	Marks	Guidance
2			**T1** Ref to HRT treatments containing oestrogen and, progesterone / progestin; **T2** Ref to timing combinations (of oestrogen and progestin); **T3** Ref to mode of delivery (of oestrogen and protestin); **T4** Ref to oestrogen only HRT following hysterectomy; **T5** Ref to phytoestrogens; *Risks* **R1** (slight) increase in risk of, breast / endometrial / ovarian cancer; **R2** (slight) increase in risk of, CHD / strokes / DVT; **R3** example of named side effect of HRT; *Benefits* **B1** prevention of, named symptoms of menopause; **B2** prevent decrease in bone density / reduce risk of, (hip) fractures / osteoporosis; **B3** reduces risk of Alzheimer's if taken before 65;	8 max	**T1 CREDIT** a reference to either or both hormones **T2** e.g combined / continuous combined / cyclical timings **T3** e.g. pills / patches / IUD device / pessary **T5 CREDIT** named examples e.g. isoflavones **IGNORE** cervical cancer **R2 ACCEPT** ref to MI, thrombosis, **R3** e.g. sickness / abdominal cramps / weight gain / PMT symptoms **B1** e.g. hot flushes / anxiety / sleep disturbance / memory loss **CREDIT REVERSE ARGUMENT** as a risk e.g. increases risk of Alzheimer's if taken after 65 **Examiner's Comments** This was one of the best answered questions on the paper with candidates displaying an extensive knowledge of the topic. While this was an AO1 question and intended to be accessible across the mark range, good answers broke down the requirements of the question and discussed the options available for treatments and then went on to discuss the risks and benefits.

Question			Answer/Indicative content	Marks	Guidance
			Total	8	

Question			Answer/Indicative content	Marks	Guidance
3		i	(in Africa) idea that people die younger but DALY is (still) high; (Africa and North America) comment on the magnitude of the difference in life expectancy and DALY; Use of data in support of either statement;	2	ACCEPT idea that the DALYs are (fairly) close but there is a larg(er) difference in life expectancy CREDIT calculations e.g. (Africa) DALYs (about) 18% less whereas life expectancy (about) 32% less OR Life expectancy in Africa is 68% of that in North America but DALYs are 81.7% IGNORE references to raw data Examiner's Comments Part **(i)** required a careful consideration of the data. Weaker candidates re-stated the question and quoted figures without any further comment.

Question			Answer/Indicative content	Marks	Guidance
		ii	(due to) more, manual labour / agricultural work / AW, in population; *idea that* start working as (young) children; more walking / poor foorwear; lack of (sufficient) protein / vitamin C, in diet;	2	IGNORE reference to more exercise or active lifestyle (choice) IGNORE general reference to malnutrition IGNORE ref to aluminium (as this is linked to osteoporosis) Examiner's Comments Many candidates were able to explain the high DALY in terms of physical work from an early age. Some candidates implied it was a lifestyle choice to undertake more physical exercise. Others drifted into a discussion of low calcium or vitamin D - forgetting that they were osteoarthritis DALYs not osteoporosis.
		iii	osteoporosis, data / figures / AW, varies with gender; ref to effect of menopause; ref to validity;	2	CREDIT idea that it will be higher in females than males DO NOT CREDIT if given as part of a list Examiner's Comments Most candidates were aware of the effect of the menopause but fewer went on to link this to differences in the incidence in males and females. Some good references to validity were seen but, as in previous session, a list such as valid, reliable and accurate was not credited.
			Total	6	

Question			Answer/Indicative content	Marks	Guidance
4			*idea that* in cyclical HRT progesterone is not given every day;	1	**CREDIT** explanations using reverse argument e.g. an implant would release hormones continuously Examiner's Comments While many candidates answered this well, some other responses were imprecisely worded in terms of how progestin and oestrogen were taken. The fact that implants release hormones continuously was the most common answer given.
			Total	1	

Question			Answer/Indicative content	Marks	Guidance
5	a	i	(age) when, periods / ovulation, stops; *idea that* this is, for non-surgical reason / due to decline in follicular activity;	2	CREDIT correct reference to absence of hysterectomy IGNORE reference to HRT Examiner's Comments There were two parts to the term in **(i)** and the mark tariff reflected this. Many candidates lost marks by failing to explain what the menopause actually was.
		ii	*idea that* one population may have more / fewer, women who, are unemployed / smoke / have a higher BMI / AW; *idea that* median not affected by, extremes / outliers OR mean is affected by, extremes / outliers / anomalies; median not affected by large numbers at one age OR mean is affected by large numbers at one age;	2	CREDIT reference to smoking, unemployment, BMI, use or oral contraception, heart disease risk factors, ethnicity etc varying between populations LOOK FOR idea that highest and lowest ages can be very different (but the mid-point will still be the same) IGNORE ref to range LOOK FOR larger numbers in one group (e.g. early menopause) affect mean / do not affect median Examiner's Comments In part **(ii)**, although some good answers were seen, many candidates simply explained how the mean was calculated or suggested it would be affected by the size of the population. Most candidates ignored the information given in the stem of Q6 concerning all the variables which would affect age and which could differ between populations. The most common correct answers referred to outliers affecting the mean but not the median.

Question			Answer/Indicative content	Marks	Guidance
	b		no / less, oestrogen / progesterone secreted; (due to damage to) follicular cells; no / less development of, endometrium / uterine lining OR FSH stays high; idea of damaged oocytes destroyed;	2	Examiner's Comments This was synoptic with Unit 4 and the question was most commonly answered in terms of cigarettes causing a drop in oestrogen production but no further detail was given in terms of the cells producing the oestrogen or the knock on effect of low oestrogen in terms of the menopause.
			Total	6	

Question			Answer/Indicative content	Marks	Guidance
6		i	D1 follicle number decreases with age / negative correlation ✓ D2 (the reduction is) exponential / a logarithmic relationship ✓ D3 rapid / AW, decline after about 40 years ✓ E1 as (some) follicles, mature / rupture / release oocytes ✓ E2 (other) follicles, disappear over time / undergo apoptosis ✓ E3 (because) oestrogen declines from about 40 years ✓	4 max	ALLOW max 2 for D and max 2 for E, marks DO NOT ALLOW idea of no change between birth and puberty Examiner's Comments The description of the data in (c)(i) was well answered by the majority of candidates. Some candidates appreciated the logarithmic scale, although many quoted figures without realising the mathematical significance of the large decreases. Most candidates focused on 50 years as the critical age decrease for follicular loss, probably linking to their knowledge of the menopause without focusing on the graph. The explanations for the loss focused on ovulation but most candidates discussed the follicles being released in ovulation. Candidates should visualise follicles and their enclosed secondary oocyte so they can appreciate the correct terminology. Some candidates stated that follicles are not maturing as women age and thus follicular number decreases and failed to see the logic of their statement that this would lead to a constant level of follicles. The majority of candidates appeared not to realise that other follicles are removed by apoptosis.
		ii	menopause ✓	1	Examiner's Comments All candidates achieved the mark for (c)(ii) with a few referring to perimenopause. There were some interesting spellings.
		iii	Any two for one mark from: change in regularity of periods heart pounding / high heart rate night sweats flushed skin / hot flushes insomnia / (increased) anxiety / depression vaginal dryness	1	Mark first two answers only Examiner's Comments All candidates attempted (c)(iii) with the majority correctly identifying one symptom. Candidates should focus on symptoms that are particularly symptomatic of the menopause and not applicable to an everyday emotional change. There were some spelling errors with 'night sweats' becoming 'night sweets' and 'hot flushes' becoming 'hot flashes'.
			Total	6	

Question			Answer/Indicative content	Marks	Guidance
7	a	i	(erectile dysfunction) is the inability to, get / maintain, an erection ✓ (infertility) is due to problems with, sperm production / release ✓	2	IGNORE sperm cannot fertilise egg unqualified ALLOW abnormal sperm / low sperm count / blocked vas deferens / cannot ejaculate Examiner's Comments This was well answered with the majority of candidates correctly describing both. Some candidates described male infertility as not fertilising an egg which did not discount the possibility of it being an egg dysfunction.
		ii	medication / diabetes / (long term) stress ✓	1	ALLOW nerve damage IGNORE too much alcohol Examiner's Comments This was well answered although many answers centred around the idea of temporary dysfunction.
	b	i	increases the risk of **CHD**, **stroke** and **breast cancer** (compared with placebo) ✓ reduced risk of hip fracture and colorectal cancer ✓ differences may not be significant / no error bars shown ✓	3	DO NOT CREDIT if colorectal cancer or endometrial cancer are included IGNORE ref to endometrial cancer ALLOW no statistical analysis / SD / SE Examiner's Comments This was well answered with most candidates scoring a mark for the increased risk with CHD, stroke and breast cancer. Some candidates that did recognise the difference between the placebo and the hip fracture/ colorectal cancer did not appreciate that this meant a reduced risk, merely discussing in terms of 'lower than placebo'. Very few candidates discussed error bars. Candidates should associate bar charts with the need for error bars to represent true differences (or not).

Question			Answer/Indicative content	Marks	Guidance
		ii	*Summary of instructions to markers:* *Read through the whole answer. (Be prepared to recognise and credit unexpected approaches where they show relevance.)* *Using a 'best-fit' approach based on the science content of the answer, first decide which of the level descriptors,* ***Level 1****,* ***Level 2*** *or* ***Level 3****, best describes the overall quality of the answer.* *Then, award the higher or lower mark within the level, according to the* ***Communication Statement*** *(shown in italics):* ◦ award the higher mark where the Communication Statement has been met. ◦ award the lower mark where aspects of the Communication Statement have been missed. • The science content determines the level. • The Communication Statement determines the mark within a level.		
			Level 3 (5–6 marks) A clear discussion of the cardiovascular and cancer risks of HRT based on previous guidance and changes that have occurred due to the new guidelines. *There is a well-developed line of reasoning which is clear and logically structured and uses scientific terminology at an appropriate level. All the information presented is relevant and forms a continuous narrative.* **Level 2 (3–4 marks)** Discussion of the cardiovascular or cancer risks of HRT based on previous guidelines and a link with changes due to new guidelines. *There is a line of reasoning presented with some structure and use of appropriate*	6	**Indicative scientific points may include** Previous guidance risks; • history of breast, endometrial or ovarian cancer • history of blood clots / thrombosis • history of heart disease / CHD / stroke • untreated high blood pressure • liver disease • irregular periods New guidelines changes; • history of CHD risk not as great • cancer risk not so high. • Stopping HRT decreases risk • More recent study • More evidence

Question			Answer/Indicative content	Marks	Guidance
			scientific language. The information presented is mostly relevant. Level 1 (1–2 marks) Discussion of HRT risk using either new guidelines or previous guidelines . *There is an attempt at a logical structure with a line of reasoning.* *The information is in the most part relevant.* 0 marks No response or no response worthy of credit.		*Do not give credit for simply repeating information in the question; it must be put into context of 'previous guidance' and 'new guidelines'.* Examiner's Comments This was well answered with most candidates discussing both cardiovascular and cancer risks. The changes due to the new guidelines were poorly integrated into the risks, with candidates often arguing against these new guidelines and thus not realising the relevance of NICE and the evidence that would have accrued to put forward the new guidelines.
			Total	12	