

# Bio Factsheet



## Manipulation and Control of Reproduction

This Factsheet covers the following specification topics:

- **Methods of birth control;**
- **The use of synthetic hormones as contraceptives;**
- **The use of hormones and drugs in treating female infertility;**
- **In-vitro fertilisation (IVF) and artificial insemination (AI);**
- **The menopause and hormone replacement therapy (HRT);**
- **The use of hormones in domestic animals;**
- **The principles of cloning.**

Moral and ethical issues of these procedures are described in the Factsheet 'Ethical issues in Advanced Biology', No ? April 2002. Students would also benefit by studying the factsheet on 'Oestrous cycles', No 57, January 2000.

### Methods of birth control

Birth control gives humans the ability to control population growth and may be essential for the future well-being and survival of the human race. The global population has been increasing exponentially. If this is allowed to continue without control, eventual overpopulation will result in global starvation.

**Exam Hint** - students are expected to know the principles of each birth control method and to be able to discuss the relative advantages and disadvantages of each method. (See Table 1).

Table 1. Summary of main birth control methods

Method	Principle	Advantages	Disadvantages	Comments
Barriers to prevent sperm from reaching egg	<b>Male condom:</b> a thin rubber sheath worn over the penis. Sperm collects in the tip at ejaculation.	Reliable and easy to obtain. Give some protection against sexually transmitted diseases. Free from clinics.	Cannot be used spontaneously and may split or leak. May reduce enjoyment of intercourse.	Effectiveness improved if used in combination with a spermicide.
	<b>Diaphragm:</b> a domed sheet of rubber which fits over the cervix.	Reliable and cheap.	May be messy and must be fitted initially by a doctor.	Should be used with a spermicide.
	<b>Spermicide:</b> a gel, cream or foam put in the vagina to kill sperm and block their entry to the uterus.	Cheap, readily available and easy to use.	Not very reliable if used alone.	Should be used in combination with other barrier methods.
	<b>Sponge:</b> polyurethane impregnated with spermicide fitted over the cervix.	Easy to use, but must allow time for spermicide to spread over cervix.	Not reliable if used alone.	Should be fitted 24 hours before intercourse and left for 6 hours after.
Hormone management to interfere with ovulation and/or implantation	<b>Combination pill:</b> Made of synthetic oestrogens and progesterone. Prevents ovulation and implantation.	Very reliable if taken regularly. Enables spontaneity. Reduces the risk of some cancers. Free from clinics	May have side effects, for example, nausea and weight gain. Can increase the risk of thrombosis.	Provides no protection against sexually transmitted diseases.
	<b>Hormone injection contraceptive:</b> prevents ovulation and thickens cervical mucus.	An injection lasts for three months. Easy to use.	May result in menstrual changes and weight gain.	Provides no protection against sexually transmitted diseases.
	<b>'Morning-after' pill:</b> Uses a high concentration of oestrogen to prevent implantation.	Used after intercourse rather than before.	Contains a high level of oestrogen which can produce unpleasant side effects such as nausea.	Unsuitable for regular use.
	<b>Contraceptive implant:</b> Implanted under skin and releases hormones to prevent ovulation.	Very reliable. An implant will last for up to 5 years.	May cause changes in menstrual pattern.	Provides no protection against sexually transmitted diseases.
Behavioural	<b>Rhythm method:</b> Avoid intercourse during fertile periods of the menstrual cycle.	No costs because it is a natural method.	Unreliable because it is difficult to determine precise times of fertility.	Kits are available for assessing times of fertility, but they are not totally reliable.
	<b>Withdrawal:</b> Penis removed from vagina before ejaculation.	No cost.	Unreliable and requires discipline to do.	
Surgical	<b>Vasectomy:</b> Vasa deferentia cut to prevent sperm passage.	Very reliable. One operation produces a permanent effect.	Generally irreversible.	
	<b>Oviduct ligation:</b> The oviducts are cut and tied.	Very reliable. One operation produces a permanent effect.	Difficult to reverse.	
Other	<b>Intrauterine device:</b> a loop or coil of plastic or copper which prevents implantation.	Allows intercourse to be spontaneous.	Can be displaced and can be uncomfortable.	Requires insertion by a doctor.

**The use of synthetic hormones as contraceptives**

- In the post-ovulatory phase of a normal menstrual cycle, high concentrations of progesterone inhibit the release of GnRF (gonadotropin releasing factor) by the hypothalamus.
- The lack of GnRF suppresses release of the gonadotropins, FSH (follicle stimulating hormone) and LH (luteinising hormone) by the anterior pituitary body, thus preventing initiation of the next menstrual cycle.
- A high concentration of progesterone also suppresses the development of immature ovarian follicles and their secretion of oestrogen. Little or no follicular growth can occur while progesterone is present in high quantity.

Birth-control pills use these inhibitory actions of progesterone. The pills contain several synthetic compounds similar to oestrogen and progesterone. The pill most commonly used, called a ‘combination pill’, contains a high concentration of ‘progesterone’ compounds and a low concentration of ‘oestrogen’ compounds. The presence of oestrogen reduces the incidence of side effects (see below). If taken regularly, the pills prevent follicle development, ovulation and implantation. Thus they prevent conception. High progesterone concentration also causes the cervical mucus to be thickened and sticky. This obstructs the movement of sperm.

As well as preventing pregnancy, oral contraceptives also have other advantageous effects. These include **reduction** in:

- **menstrual blood loss**
- **development of anaemia**
- **irregular menstrual bleeding**
- **non-malignant breast disorders**
- **cancer of the womb lining/endometrium**
- **premenstrual tension/menstrual pain**
- **formation of ovarian cysts**
- **cancer of the ovaries**
- **inflammation of the oviducts**
- **post-menopausal osteoporosis**

Set against these advantages is a slight increase in the risk of cancer of the cervix but there is no definite evidence of a significantly increased risk of breast cancer for individual women. Oral contraceptives occasionally may increase the tendency for the blood to clot, and so promote clotting in the deep leg veins (and even in arteries). Obstruction of brain arteries, leading to a form of stroke, has occasionally occurred in this way. Oral contraceptives also may raise levels of blood cholesterol.

Other possible side-effects are:

- **breast tenderness**
- **emotional upset**
- **fatigue**
- **skin changes/acne**
- **nausea**
- **weight gain**

Oral contraceptives often reduce fertility and interfere with menstrual cycles for a short time after use, but they do not cause long-term infertility. They have no measurable effect on the rate of spontaneous abortion or on the incidence of chromosomal abnormalities.

**The use of hormones and drugs in treating female infertility**

Female infertility is an inability to conceive and may be due to:

- **endometriosis** (when endometrial tissue grows outside the uterus)
- **a failure to ovulate**
- **poor egg quality**
- **polycystic ovary syndrome** (many small, abnormal cysts grow in the ovary)
- **blocked oviducts**

Failure to ovulate is a common form of infertility in women and is usually due to an hormonal problem, such as insufficient or unbalanced FSH and LH concentrations.

It can be treated by fertility drugs, for example, **clomiphene citrate** (trade names Clomid and Serophene). This drug is taken daily in pill form and prompts the hypothalamus to stimulate the anterior pituitary body to release more LH and FSH. This stimulates ovarian follicle maturation and mature egg production. If clomiphene treatment is not successful within 5 or 6 months other drugs or treatments are used.

A commonly used hormonal fertility drug is **human menopausal gonadotropin** (hMG). This is a mixture of LH and FSH and directly stimulates ovarian follicles into development to produce mature eggs. It is used in combination with the hormone **human chorionic gonadotropin** (hCG) which triggers the release of the mature eggs.

Daily injections of hMG are given for 7 to 12 days to cause the follicle maturation. On the following day an injection of hCG is given which stimulates the most mature follicle or follicles to release the egg or eggs.

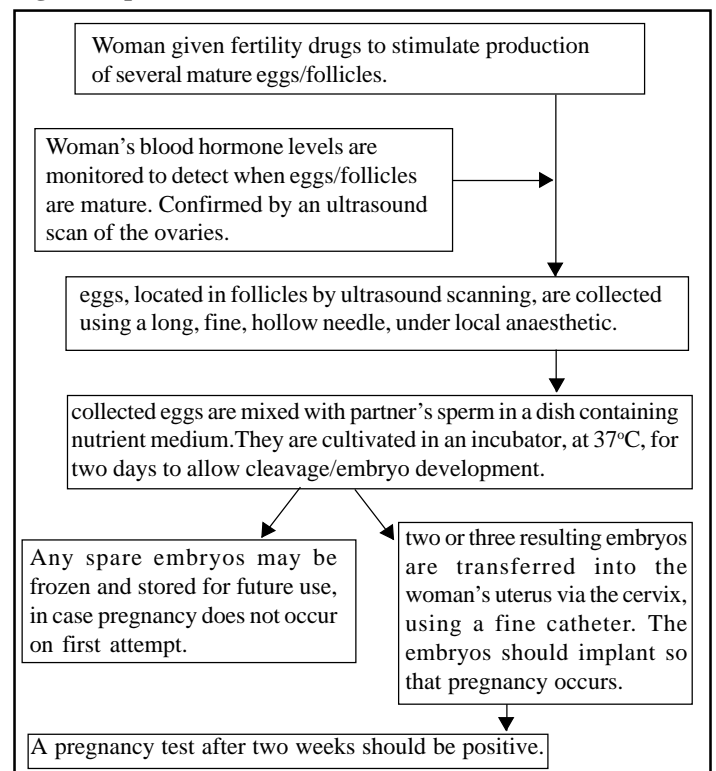
**Exam Hint** – there is considerable confusion in different biological texts about the spelling of gonadotropin (or gonadotrophin). ‘Trophos’ is greek for ‘feeding’ (eg. trophic levels) but ‘tropos’ is greek for ‘growth’ (eg. tropisms in plants). The correct spelling is ‘gonadotropin’. Remember to use the correct spelling in examinations.

**In-vitro fertilisation (IVF)**

‘In vitro’ is a Latin term meaning ‘in glass’. It refers to the glass container where fertilisation occurs. Although this is usually a dish, in the popular mind it was thought to be a test tube - thus the term ‘test-tube baby’.

In IVF, eggs are collected from the woman’s ovaries and mixed with the man’s sperm in a dish. The technique was first used successfully in 1978, since when thousands of IVF babies have been born to women with fertility problems, worldwide. The procedure of IVF is outlined in Fig 1.

**Fig 1. IVF procedure**



The technique of IVF gives women who have damaged, blocked or missing oviducts a chance of having a baby. Twins are frequently produced by IVF, but no more than 2 or 3 embryos are implanted, because of the risk of multiple births and a consequent reduction in the success rate.

IVF is also used in cattle and sheep breeding and allows the effective use of animals with a high genetic value.

**Artificial insemination (AI)**

Artificial insemination (AI) is less 'high-tech' than other methods of assisted conception. In AI, semen is placed into the woman's uterus at or near the time of ovulation, and aims to place the sperm near to the egg. It is helpful when the man has a low sperm count, or when the sperm have difficulty getting through the woman's cervical mucus. Because sperm is placed directly inside the uterus, or even into the oviducts, AI can help couples who are unable to have intercourse. The procedure is also called intrauterine insemination, or IUI.

To improve the chances of becoming pregnant by AI, the women may be treated with fertility drugs to ensure that several mature eggs are released at ovulation. Ovulation can be detected by scanning with ultrasound, or by monitoring the basal body temperature (which rises slightly at the time of ovulation). At this time, a sample of the partner's sperm is introduced through the cervix, using a fine catheter.

In cattle breeding, AI has been used for many years. It ensures that 'high quality' sperm from 'high quality' bulls fertilises eggs from 'high quality' cows. 'High quality' refers to progeny testing in which only those animals that produce healthy offspring, that become efficient milk or beef producers, are bred from. Inferior stock is not allowed to breed.

**The menopause and hormone replacement therapy (HRT)**

The menopause occurs in women usually between the ages of 45 and 54 years. At this age, over a time scale of 1 to 2 years, ovulation and menstruation cease, because of a gradual decline in oestrogen and progesterone production. This is probably because of a decreased sensitivity of the ovaries to gonadotropin stimulation. The hormonal reduction can cause unpleasant symptoms, for example, emotional stress, depression, anxiety, hot flushes, insomnia and bone loss of calcium. The bone loss can be as great as 7% per year and can lead to osteoporosis.

To minimise and delay the effects of the menopause, many (but not all) women can be prescribed low doses of synthetic oestrogen (and sometimes, progesterone also). This is called hormone replacement therapy (HRT). The bone calcium loss can also be reduced by increasing calcium intake and by increasing the frequency of moderate weight-bearing exercises, such as walking, dancing or cycling.

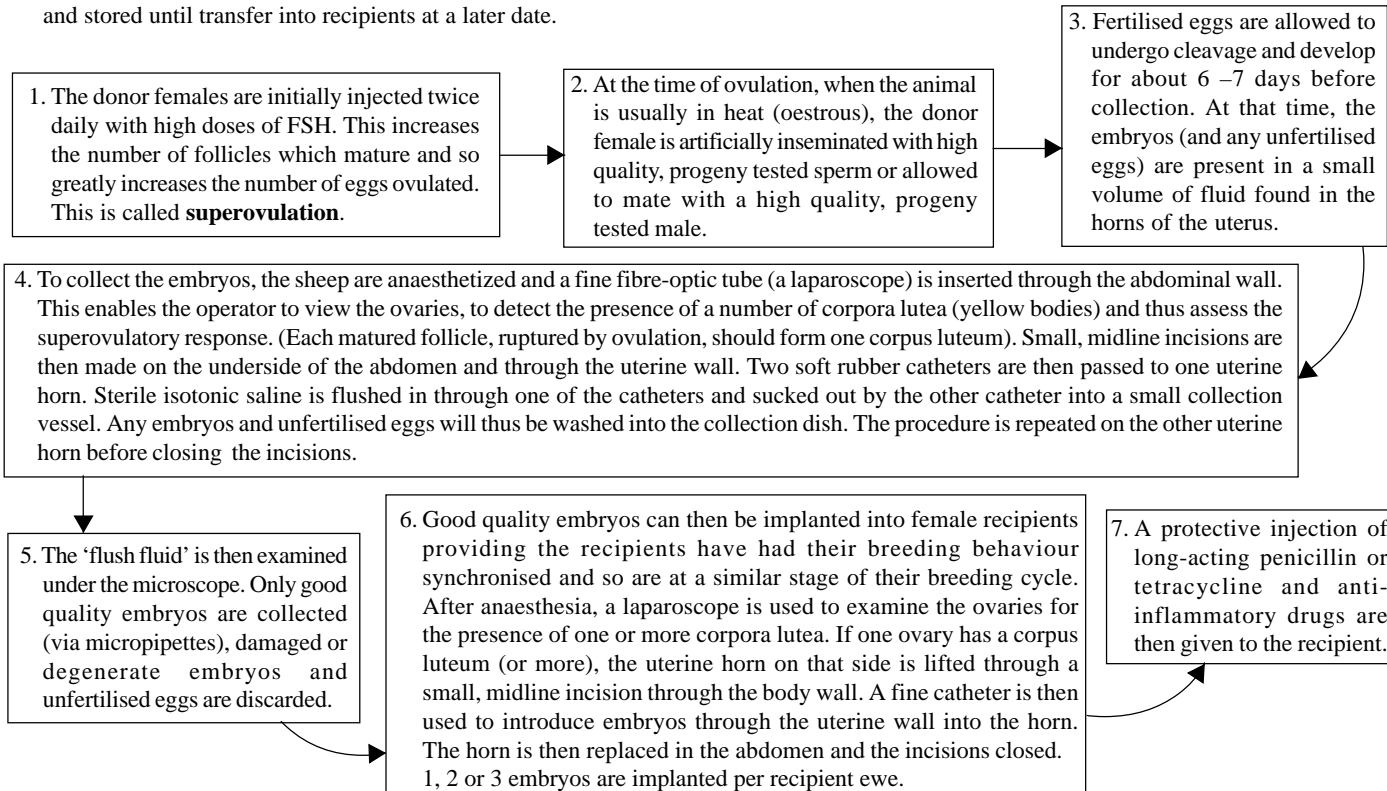
HRT, by oestrogens only, has been shown to slightly increase the chances of developing cancer of the breasts and uterus. However, the survival rate for sufferers of these cancers is higher in women who have received HRT than in women who have not. The inclusion of progesterone in the HRT decreases the chance of developing uterine cancer but means that regular menstruation tends to persist.

**The use of hormones in domestic animals**

Embryo transfer (in sheep) involves the following steps:

- recovery of embryos from the uterus of a donor female;
- the transfer of good quality embryos into the uteri of recipient (surrogate) females;
- alternatively the collected embryos can be held frozen in liquid nitrogen and stored until transfer into recipients at a later date.

*Exam Hint – questions on the use of hormones in domestic animals will probably relate to producing large numbers of embryos for transplanting (embryo transfer), synchronising breeding behaviour in sheep, or increasing milk production in cows.*



To synchronise the breeding cycles of donors and recipients, **progesterone releasing sponges** are placed in their vaginas. These contain slow release synthetic progesterones, and sometimes GnRF. They are left in place for several days, until oestrous. The high dose FSH injections (to induce superovulation) should be given to the donors starting 72 hours before the sponges are removed.

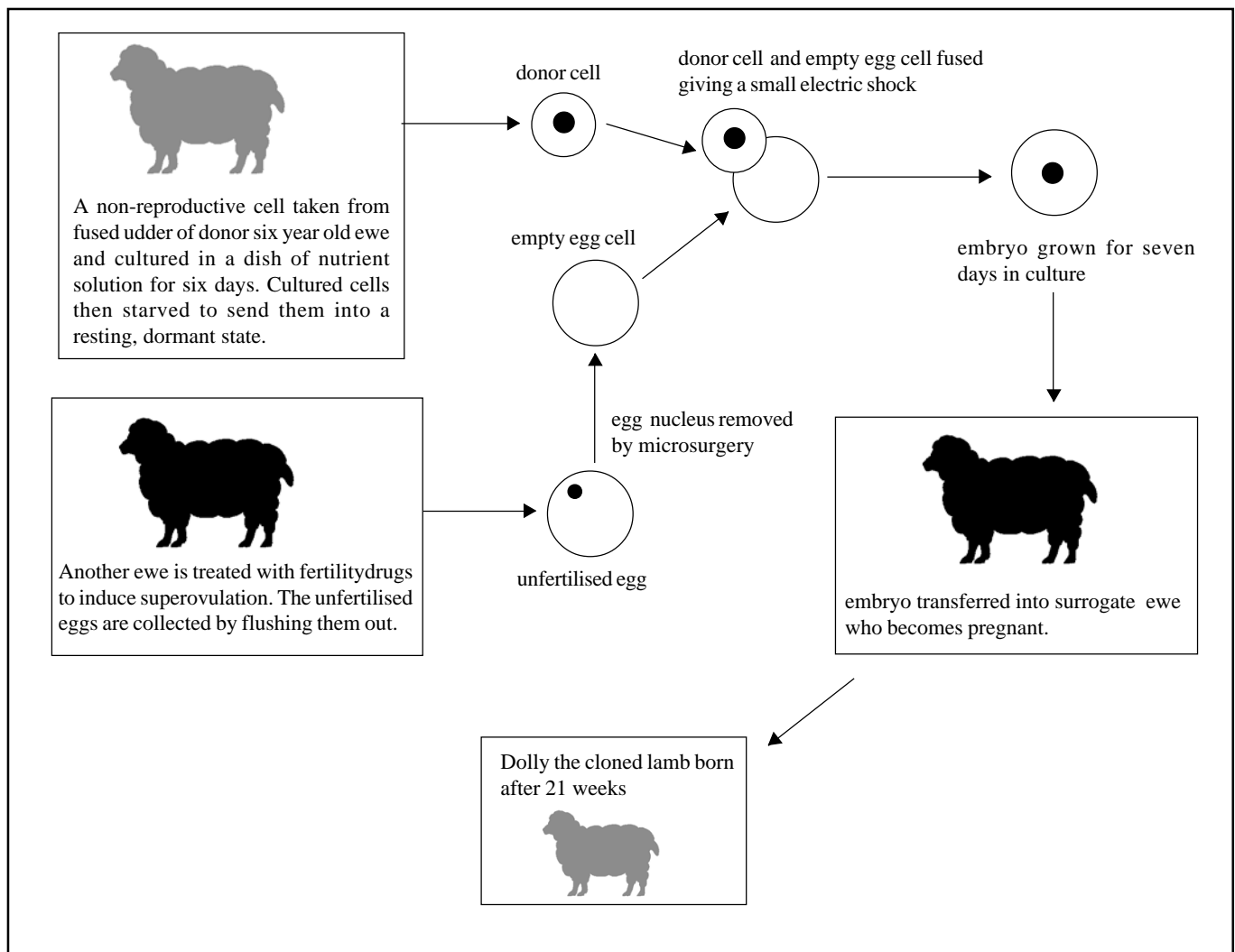
Since 1994, milk production in many dairy cows has been increased by the use of **bovine somatotropin hormone (BST)** which is a growth

hormone produced by the anterior pituitary body. BST can be manufactured in large quantities by recombinant DNA technology. Lactating cows are injected daily with the recombinant BST and as a result show a 10 to 20% increase in milk yield. This gives extra profits but causes side effects in the cows, for example, stress, an increase in disease susceptibility and in the incidence of cystic ovaries, uterine disorders, and mastitis, a decrease in birth weight of calves and an increase in the incidence of retained placentas.

**The principles of cloning**

There are two main methods of 'artificial' cloning:

1. Two or three day old embryos, which consist of only a few cells, are divided into individual cells. By incubating the cells, in a suitable growth medium, at 37°C, the individual cells can be induced to develop into separate embryos. These embryos can be transferred into surrogate mothers and should develop, through pregnancy, into normal offspring. Many sexually reproducing animals, including rabbits, sheep and toads, have been cloned by this method since its development in 1979..
2. Mammals can now be cloned from non-reproductive cells. The technique is shown in the following flow chart which illustrates how Dolly, the first sheep to be cloned by this method, was produced:



Dolly was genetically identical to the donor sheep who supplied the original non-reproductive cell. She is now several years old, has had lambs of her own, and is apparently healthy, apart from suffering from some arthritis.

Several other species of mammal have now been cloned by the same technique, including calves and pigs. Cloning will eventually be valuable to farmers because high quality animals, produced by traditional selective breeding techniques, could be cloned to give genetically identical offspring instead of the variable offspring produced by sexual reproduction.

Human cloning is considered unethical and is legally banned in Britain, the USA and most other countries of the world. However, Britain has recently made it legal, under licence, to clone cells from human embryos in order to form replacement tissues, eventually enabling repair of, for example, damaged heart muscle or damaged spinal cord. A cure for Parkinson's disease may also arise from this 'stem cell research'.

**Practice Questions**

1. Read through the following passage, which describes how Dolly, the sheep was cloned, and then fill in the spaces with appropriate words or phrases.

Scientists took a ..... cell from the ..... of a six year old ..... sheep (ewe) and cultured it in a ..... for six days. Another ewe was treated with ..... drugs to cause ..... and the eggs were collected by a flushing method. They then took one of these unfertilized eggs and removed the ..... that contains its genetic code using microsurgery.

Next, the donor cell and the empty egg were put together and given an ..... to combine them. The egg, which now contained the donor nucleus, began dividing as a fertilized egg would divide, and became an embryo. It was allowed to grow in a nutrient solution for seven days.

The embryo was .....by inserting a fine catheter through the ..... into the uterine horns of a another sheep (a recipient ewe). This ewe acted as a ..... mother, who carried Dolly through pregnancy and gave birth to her. Apart from being genetically identical to the sheep that donated the udder cell, Dolly was normal in every way. 11

2. Complete the following table about birth control, placing a tick (✓) in the box if the statement is correct or a cross (X) if the statement is incorrect.

Statement	Tick or Cross
The combination pill contains oestrogen, progesterone and GnRF	
The combination pill contains a high concentration of oestrogen and a low concentration of progesterone.	
Vasectomy and ligation of the oviducts are usually irreversible.	
Use of a condom reduces the risk of transmitting sexual diseases but use of the contraceptive pill does not.	
The only behavioural method of birth control is the rhythm method.	
The 'morning-after' pill contains a high concentration of progesterone which inhibits implantation.	

6

3. (a) Suggest three causes of infertility in women. 3
- (b) (i) Name one non-hormonal drug used to treat infertility and describe how it works. 3
- (ii) Name two hormones that are used to treat infertility in women. 2
- (c) (i) What is 'superovulation'? 1
- (ii) State three applications of the use of 'superovulation'. 3
- (d) (i) How may breeding cycles be synchronised in sheep? 3
- (ii) How may milk yield in cows be improved by hormonal treatment? 2

**Answers**

1. non – reproductive cell; udder; donor; nutrient solution; fertility; superovulation; nucleus; electric shock; implanted; cervix; surrogate; 11

2.

Statement	Tick or Cross
The combination pill contains oestrogen, progesterone and GnRF	X
The combination pill contains a high concentration of oestrogen and a low concentration of progesterone.	X
Vasectomy and ligation of the oviducts are usually irreversible.	✓
Use of a condom reduces the risk of transmitting sexual diseases but use of the contraceptive pill does not.	✓
The only behavioural method of birth control is the rhythm method.	X
The 'morning-after' pill contains a high concentration of progesterone which inhibits implantation.	X

6

3. (a) any three of: endometriosis; a failure to ovulate; poor egg quality; polycystic ovary syndrome; blocked oviducts; max 3
- (b) (i) clomiphene citrate; stimulates the hypothalamus to induce more release of LH and FSH from the anterior pituitary; this stimulates follicle maturation and mature egg production; 3
- (ii) human menopausal gonadotropin (hMG); human chorionic gonadotropin (hCG); 2
- (c) (i) when more ovarian follicles mature than normal and so produce more mature eggs than normal; 1
- (ii) any three of: to improve the chances of conception in conjunction with artificial insemination; to produce more eggs when intending to carry out IVF in women; to produce more eggs in domestic animals when embryo transplantation is intended; to produce more eggs when cloning is intended; max 3
- (d) (i) by using intra-vaginal sponges which are left in place until oestrous; contain slow-release progesterones; and sometimes GnRF; 3
- (ii) give daily injections; of (genetically engineered) bovine somatotropin (BST); 2

**Acknowledgements:**

This Factsheet was researched and written by Martin Griffin Curriculum Press, Unit 305B, The Big Peg, 120 Vyse Street, Birmingham. B18 6NF Bio Factsheets may be copied free of charge by teaching staff or students, provided that their school is a registered subscriber. No part of these Factsheets may be reproduced, stored in a retrieval system, or transmitted, in any other form or by any other means, without the prior permission of the publisher. ISSN 1351-5136