Biology EOY Notes

Topic 1: Sexual Reproduction

Clarifications

- Pre-ejaculate – a substance produced by the Cowper's gland before the real ejaculation to lubricate the urethra for the semen and neutralizes traces of acidic urine in the urethra.

Male Reproductive System (refer to exercise B1)[1]

- Kidneys (right and left) – Process blood and filter waste products and urea.
- Ureter (right and left) – Transports urine to bladder from kidney.
- Urinary bladder - To contain urine.
- Prostate gland – Gland that produces fluid and nutrients for sperm (for ejaculate). Contains a muscle that helps in the expulsion of sperm.
- Cowper's gland – Produces pre ejaculate.
- Seminal vesicle – Produces a sugar rich fluid that nourishes sperm. The secreted fluid constitutes most of the semen, and is slightly acidic (causing semen's acidic nature). This helps in neutralizing the acids present in the female vaginal track.
- Urethra – The tube that transports both sperms and urine (at different times, controlled by a valve).
- Vas deferens (aka sperm ducts)- The vas deferens is a long, muscular tube that travels from the epididymis into the pelvic cavity The vas deferens transports mature sperm to the urethra in preparation for ejaculation
- Epididymis – Storage area of sperms.
- Testis – The glands that produce sperms.
- Scrotum – The bag which holds the testis outside the body.
- Penis – Delivers semen to the female reproductive system.

Female Reproductive System (refer to exercise B1)

- Kidneys (right and left) - Process blood and filter waste products and urea.
- Ureter (right and left) - Transports urine to bladder from kidney.
- Urinary bladder – To contain urine.
- Uterus – Site where fertilized egg implants and fetus develops during pregnancy.
- Oviduct – Collects and caries the egg to the womb.
- Ovary – The female sex organ that produces the ova.
- Uterine wall – Grows a thick uterine lining which is rich with blood vessels, providing the ideal site for implantation.
- Uterine lining (endometrium)
- Cervix – An opening to the uterus, which convulses and collects semen and sends it into the uterus.

[1] http://my.clevelandclinic.org/anatomy/male_reproductive_system/hic_the_male_reproductive_system.aspx

- Vagina – It receives the male penis during sexual intercourse, provides the passageway for menstrual blood during menstruation, and serves as the birth canal for fetal offspring.
- Urethra – Transports urine from the bladder out of the body (through the vagina).
- Vulva – A collective term for the various parts that make up the female external sex organ.

Puberty

- Puberty is the stage when males and females become able to reproduce sexually.
    - Controlled by hormones produced in the pituitary gland – these hormones only affect the organs which can recognize the.
- Male Sex Organs:
    - Penis
    - Testes
- Female Sex Organs:
    - Vagina
    - Uterus
    - Ovary
- Puberty in males:
    - The production of testosterone is triggered by a pituitary hormone, and the production of testosterone causes the effects of puberty
- Puberty in females:
    - The production of oestrogen is triggered by a pituitary hormone, and the production of oestrogen causes the effects of puberty in females.
- Primary sexual characteristics involves sex organs, and the changes are necessary for reproduction.
    - Male:
        - Production of sperms begins.
    - Female:
        - Vagina and uterus grow
        - Menstruation begins
- Secondary sexual characteristics involves other body parts, and the changes are not necessary for reproduction, which are rather caused by hormonal differences during puberty.
    - Male:
        - Change in behaviour
        - Hair at armpits, pubic region, and chest, etc.
        - Voice deepens (as Adam's apple grows)
        - Oily skin
        - Growth spurt
    - Female:
        - Change in behaviour (more maternal and more attraction towards males
        - Hair at armpits, pubic region, etc.
        - Development and enlargement of breasts
        - Hips broaden, growth spurt, increase in fat.

Menstrual Cycle

Day 1 to 5: Menstruation

- Uterine lining sheds
- Broken uterine lining flows out of the vagina as a bloody discharge

Day 6 to 12: Follicular phase

- One follicle in the ovary begins to develop and produce the hormone **oestrogen**.
- Oestrogen causes the uterine lining to repair.

Day 13 to 15: Ovulation

- A mature ovum is released from one ovary at peak oestrogen levels.
- The ruptured follicle in the ovary becomes a corpus luteum
- The ovum is swept into the fallopian tube and moved along by peristalsis.

Day 16 to 28: Luteal phase

- Corpus luteum in the ovary produces the hormone **progesterone**.
- Progesterone helps to maintain the uterine lining.
- If fertilisation does not occur, corpus luteum begins to degenerate (consequently, the production of progesterone ceases).
    - Oestrogen and progesterone levels decline.
    - Therefore, the uterine lining begins to shed.

The fertile period of a woman is the days in her menstrual when she is most likely to conceive after having sexual intercourse. Ovulation occurs between days 13 and 15. The ovum is able to survive 1 day in the woman so sperms are able to fertilise the ovum as late as day 17. Sperms are able to survive up to 3 days in the woman so they can be "waiting" in the fallopian tubes as early as day 10.

Oestrogen and Progesterone

Oestrogen (produced in a graafian follicle):

- Peaks at ovulation (and levels decline immediately after, once uterine lining is at maximum thickness).
- Oestrogen causes the uterine lining to thicken.
- Produces in the ovaries (from a maturing graafian follicle)

Progesterone (produced in a corpus luteum):

- After oestrogen causes the uterine lining to reach maximum thickness, progesterone helps to maintain it at the maximum thickness throughout the luteal phase.
- Progesterone levels decline just before the menstrual phase begins (causing the shedding of the uterine lining).

Male and Female Gametes

	Male Gametes	**Female Gametes**
Size	Tail: ~0.04mm;	~0.1mm

	Head: 0.005mm x 0.003mm	
Head	Head, middle piece, tail	Disproportionally large amount of cytoplasm, jelly cot, polar bodies (nucleus)
Relative Numbers	50 million to 500 million	1
Chromosomes	X or Y	X

Processes

Ovulation – The release of an ovum from an ovary. (Occurs in the ovary)

If two ova are released simultaneously, and both are fertilized, then fraternal twins are formed.

Fertilisation – The fusing of the male and female gametes (the sperm with the ovum). (Occurs in the oviduct)

Fertilisation in humans is only restricted to a few days a month because the sperm and egg have certain lifespans, and the ovum is released only once every 28 days. Once fertilisation occurs, mitosis will occur to the fertilized cell in the oviduct before it becomes an embryo and implants itself onto the uterine lining.

If the zygote splits after the fertilisation into two identical cells, and embryonic development continues, identical twins are formed.

Embryo Development – Zygote develops into an embryo in 3-5 days in the oviduct.

Implantation – The "attachment" of an embryo (a few days after fertilisation) onto the uterine lining of the mother's uterus. (occurs in the uterus, onto the uterine lining).

Pregnancy

- Gestation period is about 40 weeks.
- Placenta – A network of blood vessels that form during implantation and start developing during implantation.
    - A network of blood vessels that forms between the uterine lining and the outer cells of the developing embryo.
    - The fetus is connected to the placenta by an umbilical cord (which allows for the transportation of vital nutrients required for embryonic and fetal to the fetus and transports toxic substances away from the body of the fetus).
    - Oxygen, nutrients and antibodies are passed from maternal to fetal blood.
    - Carbon dioxide and biological waste is passed from fetal to maternal blood.
- Amniotic Sac –A sac in which the fetus develops, consisting of the inner layer (amnion), and the outer layer (chorion)
    - Amnion: The inner membrane of the amniotic sac. It contains the amniotic fluid and the amniotic cavity, which is where the fetus will develop over the gestational period. It is ruptured at birth.
    - Chorion: Outer membrane of the amniotic sac. It is ruptured at birth.

- Amniotic Fluid: A fluid which surrounds the fetus during gestational development.
    - Regulates temperature inside the womb for optimal development of the fetus.
    - Acts as a shock absorber, and prevents fetus from external damage.
    - Protects fetus from mother's blood pressure.
    - Allows the fetus to move easily in the amniotic sac, to aid development.
    - Acts as a lubricant for delivery (when the amniotic sac breaks)
- Amniocentesis: A medical process to screen abnormalities in the fetus by screening amniotic fluid.
    - Amniotic fluid is collected in a syringe. This fluid will contain cells from the fetus, and these cells will be cultured and examined.
    - Test gives information about genetic and chromosomal mutations.

- Gonadotropin – a substance produced during pregnancy by the placenta. This substance will be present in the woman's urine, which is then detected by pregnancy kits.

Birth Control

Purpose: To prevent unwanted pregnancies.

1) Condoms
    - **Description** – For males, it is a thin cover that fits comfortably over erect penis, unless it is too small. For females, it is a plastic tube with a flexible ring at the end to make it stay in the vagina, also called a femidom.
    - **Category** – Mechanical
    - **How it works** – Acts as a barrier to prevent sperms from entering vagina during sexual intercourse, and also prevents exchange of genital fluid.
    - **Cost** – About $1 for a condom, $4 for a femidom
    - **Effectiveness** – About 80%
    - **Duration** – Use and dispose with each act of intercourse
    - **Protection from STIs** – Yes, as it prevents exchange of genital fluid. However, there is no guaranteed protection due to accidents such as condom breaks/slips.
    - **Disadvantages** – Irritation due to latex allergy. Requires cooperation from both sides, as it may reduce sexual pleasure.
2) Copper IUD (Intrauterine Device)
    - **Description** - IUD is inserted into uterus by healthcare provider
    - **Category –** IUD (Intrauterine Device)
    - **How it works –**It irritates the uterine lining, and prevents it from thickening. As it is not thick enough, the embryo will not be able to implant itself onto the uterine lining.
    - **Cost –** $175 to $950, lasts till 12 years
    - **Effectiveness –** 99%
    - **Duration –** Effective for 10 – 12 years
    - **Protection from STIs -** No, as semen is in contact with woman, and the woman's fluids (e.g. cervical mucus) are also in contact with the male

- **Disadvantages -** Increased bleeding and cramping in the earlier periods, after inserting IUD, but these cramping and bleeding lessens over time

3) Diaphragm
    - **Description –** Flexible rubber cap inserted into vagina and fits comfortably over cervix. Can be obtained from healthcare provider. Usually used with spermicide. Fitted in before intercourse and only taken out 6 hours afterwards
    - **Category –** Mechanical
    - **How it works –** Acts as a barrier to prevent sperms from entering uterus
    - **Cost –** $15 to $75, lasts till 2 years
    - **Effectiveness –** About 80%, safer with spermicide though
    - **Duration –** Use with each act of intercourse, reusable
    - **Protection from STIs –** No, semen is still ejaculated, male also in contact with woman's fluids
    - **Disadvantages –** Irritation due to latex allergy, increased risk of vaginal infection
4) Emergency Contraception (Pill)
    - **Description –** Taken up to 5 days after unprotected SEX
    - **Category –** Hormonal
    - **How it works –** Hormones in pill stop ovulation, cause cervical mucus to thicken so as to prevent sperm from entering uterus. It also thins the uterine lining, and thus, makes it difficult for implantation
    - **Cost –** $10 to $77 per prescription
    - **Effectiveness –** About 80%
    - **Duration –** Use after each act of unprotected SEX
    - **Protection from STIs –** Again, no
    - **Disadvantages –** Nausea and vomiting, Abdominal pain, sore breasts, irregular bleeding and headaches
5) Tubal Ligation
    - **Description –** The fallopian tubes are cut and tied. Done under general anesthesia, in a hospital. 2 incisions are made just below the naval, to access the oviducts
    - **Category –** Sterelisation
    - **How it works –** It blocks the fallopian tubes so the sperm cannot reach the egg and the egg cannot reach the uterus. Prevents fertilization
    - **Cost –** $1500 to $6000 for operation
    - **Effectiveness –** 99% (actually hundred, but there are exceptions, e.g. operation not successful or oviduct grows back)
    - **Duration –** Permanent
    - **Protection from STIs –** No
    - **Disadvantages –** Invasive surgery. May have complications from anesthesia and surgery. Irreversible.
6) Hormonal IUD
    - **Description –** IUD inserted into uterus by healthcare provider.
    - **Category –** IUD

- **How it works –** Like Copper IUD, but contains progestin, which helps prevent ovulation, and cause cervical mucus to thicken, preventing sperms from entering uterus
- **Cost –** $250 to $950 (lasts for 7 years max)
- **Effectiveness –** 99%
- **Duration -** Effective for 5-7 years
- **Protection from STIs –** NO
- **Disadvantages –** May cause irregular periods, as it disrupts ovulation

7) The "Pill"
    - **Description –** Daily medication taken by female
    - **Category –** Hormonal
    - **How it works –** Hormones in pill prevents ovulation and cause cervical mucus to thicken, blocking sperm from reaching uterus
    - **Cost –** $15 to $50 every month
    - **Effectiveness –** 92%
    - **Duration –** Taken for 21 days, rest 7 days, during the rest days, contraceptive protection is still present
    - **Protection from STIs –** NOOOOOO
    - **Disadvantages –** Nausea and vomiting. Abdominal pain, tender breasts, irregular bleeding and headaches. Easy to forget taking pills (if forgotten for more than 12 hrs, contraceptive protection will be reduced
    - About the same as the emergency pill, though less effective. May be cheaper, depending on frequency of sex
8) Rhythm method
    - **Description –** Avoid having unprotected sex during fertile period of woman
    - **Category –** Natural
    - **How it works –** Keep sperm out of vagina during fertile days of female, so the sperms only enter when the ovum is dead, so no fertilization occurs. Can be tracked by body temperature, amount of cervical mucus, and keeping track of previous periods
    - **Cost –** FREE
    - **Effectiveness –** About 75%
    - **Duration –** Track daily
    - **Protection from STIs –** NOOOOOOOOOOOOOOOOOOOOOOOOOO
    - **Disadvantages –** No side effects, however, it may be difficult to adhere to as it requires discipline and cooperation and couples may want to have sex during fertile period
9) Spermicide
    - **Description –** Comes as cream, foam, gel, film, or suppository (vaginal suppository, inserted into vagina as solid and melts or dissolves in vagina)
    - **Category –** Chemical
    - **How it works –** Kills or inactivates sperm, preventing them from fertilizing ovum
    - **Cost –** $8 per package
    - **Effectiveness –** About 71%, better if used with diaphragm or sponge

- **Duration –** Use every time you have sex
- **Protection from STIs –** NOOOO, actually, increases chances of getting STI
- **Disadvantages –** Nonoxynol-9, a common ingredient, is known to increase use of HIV and other STI transmission. Frequent use also induce lesions and ulcerations to genital mucosa lining, which increases transmission of infection agents

10) Sponge
    - **Description –** Inserted into vagina before sex, then left in vagina for at least 6hrs after sex
    - **Category –** Mechanical
    - **How it works –** Covers the cervix, blocks sperms from entering uterus, also used with spermicide
    - **Cost –** $9 to $15 for pack of 3
    - **Effectiveness –** 64 to 84%
    - **Duration –** Used and disposed with each time you have sex
    - **Protection form STIs –** NO
    - **Disadvantages –** Increased risk of vaginal infection if left in vagina for too long
11) Vasectomy
    - **Description –** Healthcare provider numbs the area around scrotum and makes an incision into the scrotum to cut and tie the vas deferens
    - **Category –** Sterelisation
    - **How it works –** Vas deferens are tied, cut, or severed, to prevent sperms from mixing into semen, so sperms do not get ejaculated into vagina
    - **Cost –** $350 to $1000 for consultation and procedure
    - **Effectiveness –** 99%, should be hundred, but it's the same case as tubal ligation
    - **Duration –** Permanent
    - **Protection from STIs –** NO
    - **Disadvantages –** Possible short-term tenderness or bruising around scrotum area after procedure. Irreversible
12) Withdrawal (coitus interruptus)
    - **Description –** Men must know when they are about to ejaculate, and then pull out penis before semen comes out
    - **Category –** Natural
    - **How it works –** Prevents semen and sperm from entering vagina, hence, no fertilization
    - **Cost –** FREEEEEEEEEEEEEEE
    - **Effectiveness** – About 80%
    - **Duration –** With each time you have sex
    - **Protection from STIs –** No, due to penis having contact with vaginal fluids (cervical mucus) and men may have pre-ejaculate
    - **Disadvantages –** Requires strong willpower from man, and it will reduce sexual pleasure (no orgasm), causing frustration. Also, pre-ejaculate may contain sperms

Alternate Set of Notes for Birth Control

1. Condoms – prevent fertilisation

    a. Placed over the erect penis or inside the vagina (with open end at vagina and the condom covering the vaginal walls).
    b. Male condom - collects semen during sexual intercourse. Coated with spermicide on the inside to kill off sperms when collecting them. Prevents exchange of genital fluids.
    c. Female condom – prevents semen from entering uterus by trapping it in the condom placed in the vagina. Also has spermicide on the inside to kill of the sperms collected. Also prevents exchange of genital fluids.
    d. Offers protection from STIs, but it is not guaranteed (broken/slipped condom)
    e. Cost effective ($1 per male condom, and $4 per female condom)
    f. Side effects – irritation due to latex allergy or spermicide
2. Copper Intra Uterine Device (IUD) – prevents implantation
    a. The copper IUD is placed into the uterus, where it constantly irritates the uterine lining, preventing it from thickening.
    b. Is a form of investment in birth control– expensive, but lasts long ($175 - $900, but lasts 12 years).
    c. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
    d. Side effects – increased bleeding and cramping initially (especially during menstruation)
3. Hormonal Intra Uterine Device (IUD) – prevents implantation
    a. Irritates the uterine lining, preventing it from thickening enough for implantation (similar to copper IUD).
    b. Also contains hormones (progestin), which is released to keep ovaries from releasing eggs (prevent ovulation), and causes the cervical mucus to thicken. When cervical mucus thickens, sperms cannot go beyond the cervix due to blockage by thick mucous.
    c. Is a form of investment in birth control– expensive, but lasts long ($250 - $950, but lasts 7 years).
    d. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
    e. Side effects – may cause disruption to menstrual cycle and irregular periods.
4. Diaphragm – prevents fertilization
    a. Is a hemispherical “cup” which is coated with spermicide placed at opening of cervix.
    b. Prevents sperm from entering uterus from vagina.
    c. It has to be changed with each act of intercourse (reusable)
    d. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
    e. Side effects - irritation due to latex allergy, and increased risk of vaginal infection.
5. Emergency Contraception – prevents ovulation and implantation (used after unprotected intercourse)
    a. Hormones in emergency pill stop ova from being released by the ovary, and causes cervical mucus to thicken, preventing sperm from entering the uterus.
    b. Cost effective (cost of the consultation and prescription).

    c. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
    d. Side effects – nausea and vomiting, abdominal pains, sore breasts, irregular bleeding, and headaches.
6. Tubal Ligation – prevents fertilisation (permanent birth control)
    a. Oviduct is cut off and tied, preventing the ova from going through the remaining parts of the oviduct, and preventing fertilisation.
    b. Cost heavy ($1500 - $6000 for consultation/operation)
    c. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
    d. Side effects – mildly invasive surgery might cause complications from anaesthesia and surgery. It is irreversible.
7. Vasectomy – prevents fertilisation (permanent birth control)
    a. Sperm ducts are tied, cut, or sealed, preventing sperms from entering semen. Therefore, there will be ejaculation, but no sperm in the semen.
    b. Cost heavy, but investment - $350 - $1000 for consultation/procedure.
    c. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
    d. Side effects – possible short term tenderness or bruising after procedure.
8. Withdrawal (pull out) – prevents fertilisation (natural birth control)
    a. The male pulls out his penis out of the vagina before he ejaculates, preventing the sperms from entering the body of the woman.
    b. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
    c. Side effects – Man may not have enough willpower/concentration to withdraw his penis in time. May reduce sexual pleasure , causing frustration and anxiety.
9. Pill – prevents ovulation, and fertilisation (even if ovulation occurs)
    a. Hormones in pill keep ova from being released, and causes cervical mucus to thicken to block sperm from entering uterus.
    b. Pills have to be taken every day.
    c. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
    d. Side effects –nausea and vomiting, abdominal pains, tender breasts, irregular bleeding, headaches, forgetting to take pills daily might cause pregnancy
10. Rhythm method – natural birth control, prevents fertilisation
    a. Body temperature, cervical mucus calendar and menstrual calendar is tracked.
    b. Women engage in sexual intercourse only on days in the non-fertile period.
    c. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
11. Sponge – prevents fertilization.
    a. Placed under the cervix opening (similar to the diaphragm)
    b. Is a sponge containing spermicide, which will absorb the semen containing the sperms and will prevent it from entering the uterus, therefore preventing fertilisation
    c. Must be used and disposed with each act of intercourse

d. Allows for exchange of genital fluid during sexual intercourse, and hence offers no protection from STIs.
e. Side effects – increased risk of infection if sponge is left in vagina for too long.

Assisted Reproductive Technologies (Refer to sample questions)

Overview

Methods:

- In-Vitro Fertilization (IVF)
  - Zygote Intrafallopian Transfer (ZIFT)
  - Intracytoplasmic Sperm Injection (ICSI)
- Gamete Intrafallopian Transfer (GIFT)
- Artificial Insemination (AI)
  - Intravaginal Insemination (IVI)
  - Intracervical Insemination (ICI)
  - Intrauterine Insemination (IUI)
  - Intratubal Insemination (ITI)
- Surrogate Mothers and Gestational Carriers
- Sperm Donors and Egg Donors

Key Definitions

Infertility : The inability to to conceive after a year of regular unprotected intercourse. Infertility can be affected by heavy workloads, stress, environmental pollution, etc.

ICSI: Intra Cytoplasmic Sperm Injection

ICI: Intra Cervical Insemination

IUI : Intra Uterine Insemination

ITI : Intra Tubal Insemination

IVI : Intra Vaginal Insemination

In Vitro Fertlization

IVF (has 2 variations, ZIFT and ICSI, but there is little difference; only in step 3):

1. Ovarian Stimulation – Woman takes ovulation drugs (FSH hormone, given over 8 to 14 days) to simulate the ovaries to produce multiple ova (in multiple follicles) at the same time. The developing follicles are monitored by ultrasound scans and measuring of blood oestrogen levels.
   a. The reason for stimulating multiple ova is that some will not develop normally after ova retrieval, and having multiple ova ready increases the chances of pregnancy.

2. Ova retrieval – An ultrasound probe is inserted into the vagina to identify and locate mature follicles. A needle, guided by probe (the probe identifies mature follicles in the ovary), pierces the vaginal wall to reach the mature follicles to aspirate (remove) the ova. The retrieval occurs 34-36 hours after ovarian stimulation, and just before ovulation.
    a. Ova retrieval is a minor surgical procedure with anaesthesia
3. Insemination – Retrieved ova are examined and the best quality of matured ones are selected. Semen is obtained from the man by ejaculation or via a special condom used during sexual intercourse. Sperms are separated from the semen and viable, motile ones are identified and isolated.
    a. Without ICSI (ZIFT)– sperm and ova are incubated together on a petri dish overnight.
    b. With ICSI – single viable sperm is injected directly into the ova.
4. Fertilisation – Fertilisation of ova occurs *in vitro* when one sperm penetrates one ovum on a petri dish (not *in vivo)*, successfully fertilized ova (zygotes) can be identified by the observation of two pronuclei (the result of the fertilisation) when viewed under the microscope after.
5. Embryo Culture – The zygotes are left to grow for up to six days, where they eventually become embryos.
6. Embryo Transfer – Embryos are screened, and up to a few of the best embryos are selected. The selected embryos are transferred directly into the uterus via the cervix with a transfer catheter.

Reasons for IVF:

- Blocked, damaged or absent fallopian tubes
- Endometriosis (abnormalities with the endometrium)
- Sperm defects, low sperm count, low sperm motility.

Artificial Insemination

1. Semen is obtained from the man by ejaculation or via a special condom used during intercourse.
2. For IUI and ITI, sperms are separated from the semen and viable, motile sperms are identified and isolated.
3. A woman's menstrual cycle is closely observed by (in order to determine the day in which ovulation occurs):
    a. Tracking basal body temperature (lowest temperature attained by the body during rest)
    b. Tracking changes in vaginal/cervical mucus
    c. The use of ovulation kits (kits that indicate the day of ovulation by screening vaginal secretion)
    d. Ultrasound tests that check for mature follicles.
    e. Blood tests to monitor blood oestrogen levels.
4. Insertion of sperms:
    a. IVI – Unwashed semen is inserted into the cervix by a catheter.
    b. ICI – Unwashed semen is inserted into the cervix by a catheter
    c. IUI – Washed sperms are inserted through the cervix into the uterus.

d. ITI – Washed sperms are injected directly into the fallopian tube.

GIFT

Very similar to ZIFT, just that the fertilisation occurs in vivo (inside the body), in one of the fallopian tubes. The woman must have at least 1 functional fallopian tube.

1. Ova Stimulation
2. Ova Retrieval
3. Sperm Retrieval
4. Insertion of gametes into one of the fallopian tubes.

Sperm Donors/Sperm Banks

Sperm donors undergo extensive medical and genetic screening (including testing for STIs, AIDS, etc.). Following, healthy viable sperms will be frozen and quarantined for 6 months at a sperm bank. Sperms will be released for use only if all tests for abnormalities are negative.

Only used if the male is unable to produce sperms.

Surrogacy and Gestational Carriers

Surrogate (has biological relations to child): Ova donor

- Pregnancy is carried by the surrogate mother (whose ova is used)
- Achieved through insemination alone or through ART.

Gestational Carrier (no biological relations to child):

- Pregnancy carried by another woman.
- Ova from infertile woman(wife) is fertilized with husband's sperm, and is transferred to gestational carriers' uterus.

<u>Sexually Transmitted Infections</u>

Syphilis (caused by bacteria)

- 3 prominent stages:
    - Stage 1: Painless sore, known as *chancre*, appears on sex organs (for 10 to 90 days). Disappears with or without treatment.
    - Stage 2: Non itchy rashes appear on other parts of the body (2 to 6 months after infection). Disappears with or without treatment.
    - Stage 3 (latent stage): No symptom for up to 10 to 20 years.
    - Stage 4 (late stage): Paralysis, blindness, insanity, heart disease, and bone/joint deformity.
- Treatment:
    - Curable at stage 1, 2, and 3 (latent), if treated quickly upon diagnosis.
    - Treated with antibiotics.
- Means of Transmission:

- Direct contact with syphilis sores (which mainly occur on sex organs/anus).
- Commonly occurs during unprotected sexual intercourse.
- Pregnant women may pass infection to fetus.

Gonorrhoea (caused by bacteria)

- Signs and symptoms:
  - Painful burning sensation when passing urine.
  - Pus discharge from penis or vagina.
  - May spread to other surrounding organs (like prostate and testis in male, and oviduct and ovaries in female)
  - May result in sterility if left untreated.
- Treatment:
  - Curable if treated quickly upon diagnosis.
  - Treated with antibiotics.
- Means of transmission:
  - Infection can be spread by contact with the mouth, vagina, penis, or anus/
  - Commonly occurs during unprotected sex.
  - Untreated mothers may pass the infection to their newborn infants, therefore causing eye infections and blindness.

AIDS (caused by virus, HIV)

- Signs and symptoms:
  - Stage 1: Upon infection, minor flu like symptoms (or no symptoms at all). No further symptoms for up to ten years. (Immune cells are gradually being destroyed).
  - Stage 2: Full blown AIDS:
    - Kaposi's sarcoma
    - Weight loss/ loss of apetite
    - Prolonged fatigue
    - Swollen lymph nodes
    - Fever/Diarrhoea
- Treatment:
  - No cure or vaccine for AIDS. Antiviral treatment slows down the progression from HIV positive status to full blown AIDS
- Means of transmission:
  - Unprotected sex from infected person (when there is genital fluid exchange)
  - Contact with infected persons' blood.
  - From mother to child during pregnancy or child birth.
  - Sharing syringes while injecting drugs.

Topic 2: Heredity

Key Definitions

- Homozygous – Having two identical alleles for a given gene (either homozygous dominant or homozygous recessive)
- Heterozygous – Having two different alleles for a given gene (1 dominant, 1 recessive)
- Homologous chromosomes – Chromosomes pairs that are of the same length, that possess alleles of the same genes. (One homologous chromosome is inherited from the mother, and another from the father)
- Mitosis – A process of one-stage nuclear division. This process forms two daughter cells from a single parent cells (with the same number of chromosomes)
- Meiosis – A two stage cell division only in sexually reproducing animals, which produces gametes with half the number of chromosomes from the original cells.
- Haploid – A cell containing a single set of chromosomes (gametes – sperm of ovum)
- Diploid – A cell containing two sets of chromosomes, with one set from each parent (all somatic (body) cells except for gametes).
- Gene – A unit of inheritance, a small segment of DNA in a chromosome, where specific genetic information is stored.
- Allele: Different forms of the same gene (either dominant or recessive for non-continuous variation)
- Phenotype - Observable traits caused by genes.
- Genotype – Genetic constitution of an organism
- Test cross – An experimental cross to determine whether an individual of unknown genotype that shows dominance for a trait is either homozygous dominant or heterozygous.
- Codominance – In heterozygotes, it is a simultaneous expression of a pair of non-identical alleles that specify different phenotypes.
- Continuous Variation – All organisms within the species shows the characteristic, but to a different extent. The extent can be any value within a range. Some can be affected by environment (e.g. height)
- Discontinuous Variation – Distinct categories, no range. Usually result of genes only, not the environment. The organism either has it, or does not have it. (e.g. Blood type)
- Mutation – A sudden change in the gene or chromosome structure or number
- Recombinant – An organism that contains a different combination of alleles from either of its parents.
- Imperfect dominance – Where the two phenotypes co-exist, but to an imperfect extent. (For example, if a white and red flower were mated, a flower with some fully white petals and some fully red petals would be an example of codominance, while a flower with all pink petals would be an example of imperfect dominance.

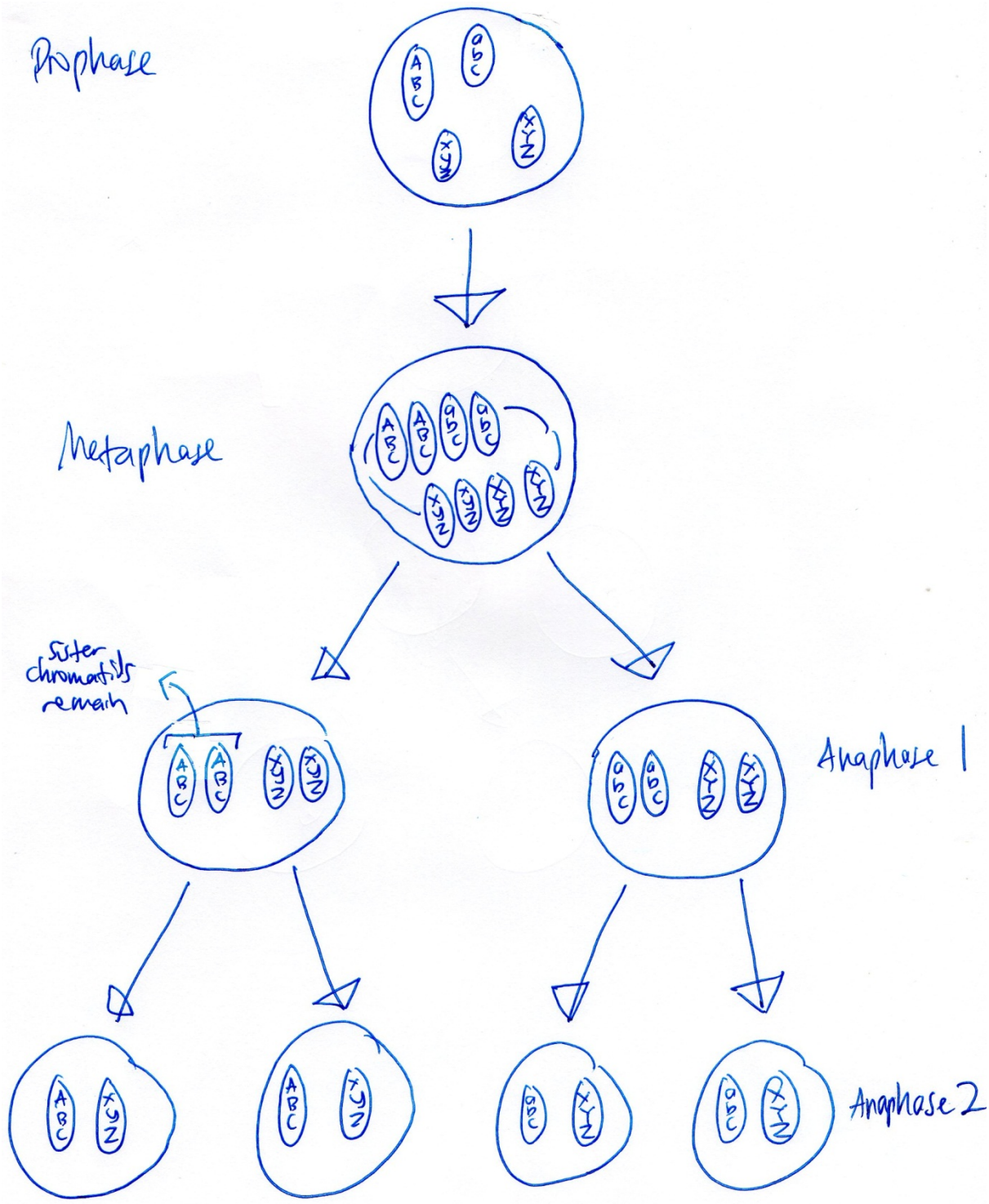
Mitosis and Meiosis

Characteristics	**Mitosis**	**Meiosis**
Purpose	Growth and repair of diploid somatic cells	Production of haploid gametes
Number of Daughter Cells	2	4
Variation	No	Yes (due to crossing over and independent assortment)
Number of Chromosomes	46	23
Location	In all somatic (but not in	Testes (in males), Ovaries (in

	gametes) cells.	females)

Meiosis occurs in the production of gametes during sexual reproduction. A total of 4 daughter cells are produced from a single parent cell. The daughter cells are haploid, that is, have half the number of chromosomes that one would expect to find in a regular somatic and non-gamete cell. In humans, each daughter cell produced by meiosis would only contain 1 set of chromosomes (23 chromosomes).

Role of Meiosis in fertilisation: The male and female gametes' nuclei fuse to form a diploid zygote. During meiosis, both male and female gametes are haploid. Meiosis has an important role in the fertilisation process because it ensures that the zygote formed has the correct number of chromosome of the species it belongs to by initially reducing the number of chromosomes in the gametes by half.



Meiosis:

1. Prophase:
    a. There are 46 chromosomes to begin with, in a single cell. 23 of these chromosomes are unique, and each of these 23 non-homologous chromosomes, have 1 chromosome each that is homologous.
    b. Chromosome Replication: The chromosomes replicate themselves, forming 4 sets of 23 chromosomes per cell. The replicated chromosome sets (daughter chromosomes) are still attached to the parent chromosome

    c. Chromosome Pairing: As such, each chromosome pairs up with the other chromosome that is homologous to it, while the two homologous chromosomes may contain different alleles. [The two chromosomes go extremely close to each other]
2. Metaphase:
    a. Homologous chromosomes are aligned at metaphase plate, and separated into sister pairs. In other words, the chromosomes will be aligned such that all chromosomes containing genes for A, B, and C will be next to each other while chromosomes containing X, Y, and Z will be next to each other as well, but below the above pair.
3. Anaphase I:
    a. The homologous chromosomes separate while the sister chromatids remain. In other words, the homologous chromosome (with different alleles for that gene) will separate into 2 cells, while the replica (sister chromatid) still remains)
4. Anaphase II:
    a. Sister chromatids separate from one another as well – causing each cell to have only 1 set of chromosomes (23 chromosomes).
    b. This allows for 46 chromosomes when two of these gametes with 23 chromosomes fuse with one another.

Mitosis:

1. Prophase (in mitosis, no pairing occurs):
    a. There are 46 chromosomes to begin with, in a single cell. 23 of these chromosomes are unique, and each of these 23 non-homologous chromosomes, have 1 chromosome each that is homologous.
    b. All these chromosomes are arranged in a single file, and then duplicate, providing two clear sister chromatids.
    c. No pairing occurs!
2. Metaphase:
    a. Chromosomes align at the metaphase plate and microtubules equally separate the DNA.
3. Anaphase:
    a. Sister chromatids separate during the anaphase, and the two chromosomes move to opposite poles of the cell, before the cell divides into two.
    b. As a result, two cells with 46 chromosomes (23 pairs) are formed.

During meiosis, 2 processes occur, that cause variation – crossing over, and independent assortment.

<u>Variation</u>

All these methods of variation cause recombinant organisms which vary.

Crossing Over (During meiosis)

As the homologous chromosomes are paired during meiosis, they are situated very close to each other, until a chiasma (a cross over point) is formed, where there will be transfer of alleles from one homologous chromosome to the other. This occurs in the prophase of meiosis, when the homologous chromosomes are still in pairs.

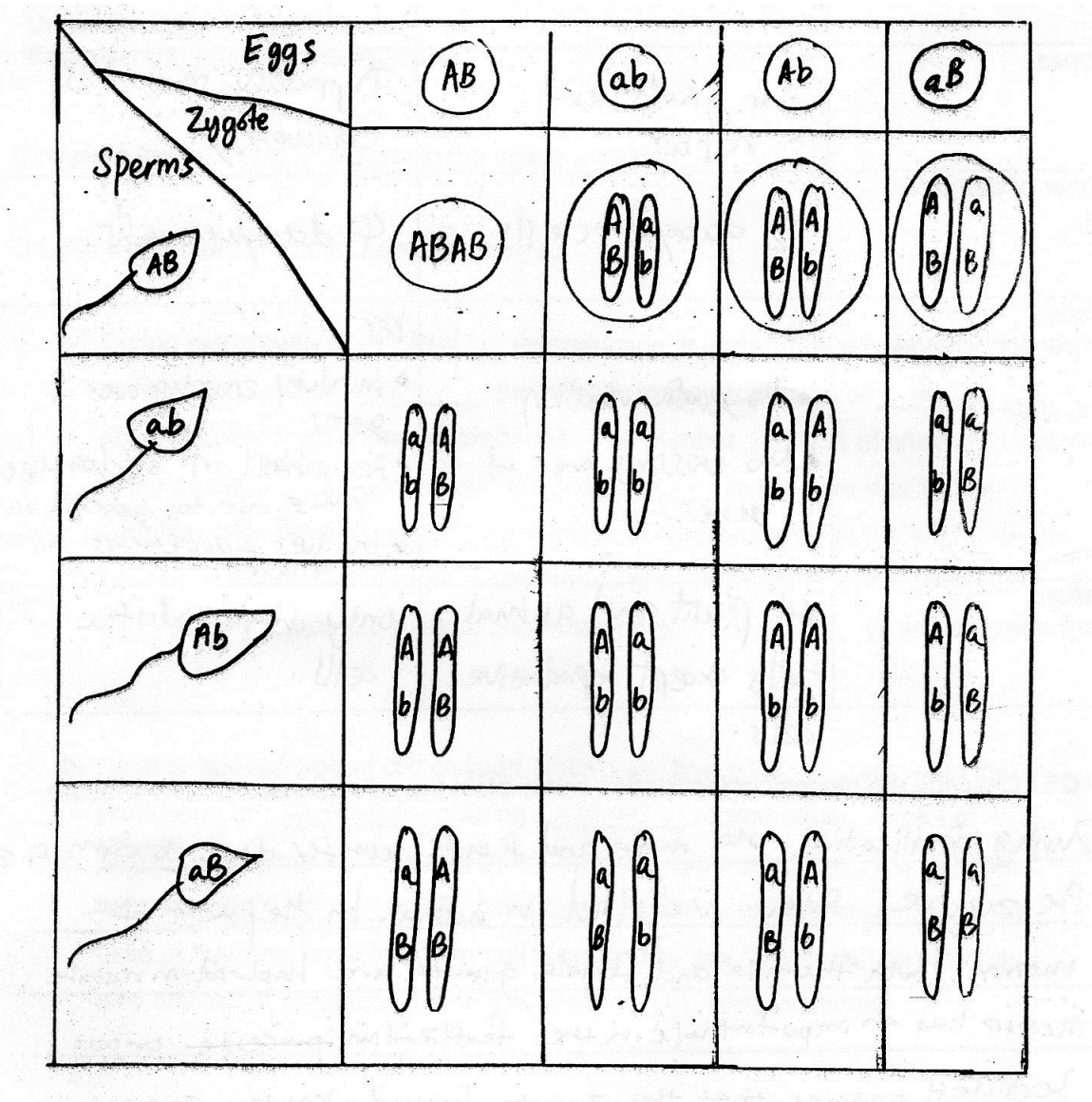
This form of variation does not occur in mitosis, because crossing over only occurs between paired homologous chromosomes (which have different alleles). Homologous chromosomes are only paired in meiosis, while in mitosis, they are only arranged in a single file before replication. Hence, crossing over does not occur in mitosis.

Independent Assortment (During meiosis)

While the homologous chromosomes in pairs are being arranged under one another (in pairs of sister chromatids, as the sister chromatids do not leave one another until the anaphase). The 1st pair of sister chromatids of the 1^{st} chromosome might be above the 2^{nd} pair of sister chromatids of the 2^{nd} chromosome. As such, there is a 1 in 2 chance of variation (when comparing 2 chromosome pairs), so there will be much more variation when comparing 23 different chromosome pairs.

Random Fertilisation (During fertilisation)

After the gametes have been formed by meiosis, there might be even more variation due to random fertilisation. Due to crossing over and independent assortment, there might already be countless permutations of allele variations in the sperm and ovum. A sperm of any permutation can fertilise an ovum of any permutation, further increasing the amount of variation between offspring.

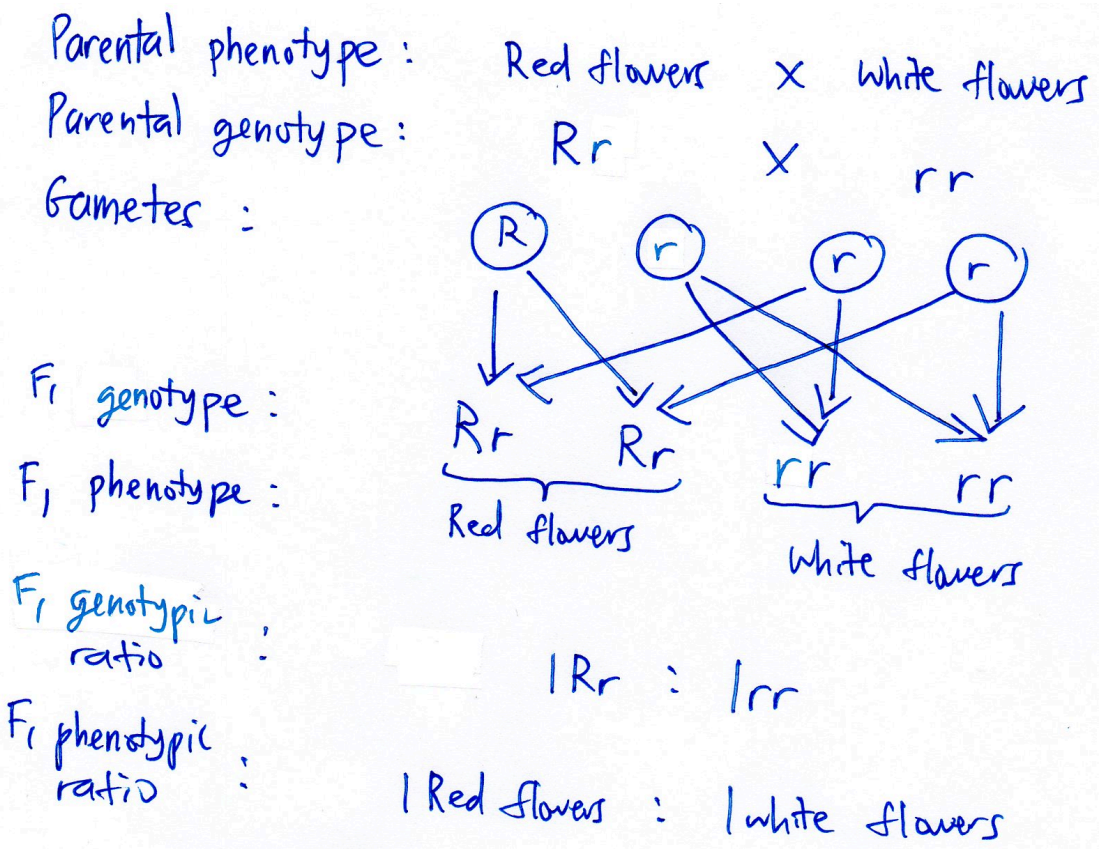


General Notes

- When depicting different alleles of the same gene, use a capital letter for dominant allele of the same gene, and a lower case letter for a recessive allele of the same gene.
    - Different alleles of the same gene must be represented by the same letter.
    - Different alleles can be capitalized differently (capital for dominant, lower case for recessive)
- For sex linked traits, use X to represent the x chromosome and Y to represent y chromosome.
    - Use a capital letter in subscript to show the dominant allele of the gene which represents a sex linked trait.
    - Use a lower case letter in superscript to show the recessive allele of the gene which represents a sex linked trait.

Genetic Diagram

Strictly follow the format given.



Punnet Square

Strictly follow the format given.

Parental phenotype = Father : Colour blind
Mother : Normal vision

Parental genotype = $X^bY \times X^BX^b$

	X^b	Y
X^B	X^BX^b	X^BY
X^b	X^bX^b	X^bY

50% of children will be colour blind
50% of female children will be colour blind
50% of male children will be colour blind
100% of female children will be carriers
⋮

} Depends on question

Monohybrid Inheritance

Ratio Table (Refer to this to understand phenotypic and genotypic ratios):

Parental Phenotype	Phenotypic Ratio (Dominant : Recessive)	Genotypic Ratio (Homozygous Dominant: Homozygous Recessive: Heterozygous
Both Homozygous Dominant	All Dominant	All Homozygous Dominant
Both Homozygous Recessive	All Recessive	All Homozygous Recessive
Both Heterozygous	3:1	1:1:2
1 Homozygous Dominant, 1 Homozygous Recessive	All Dominant	All Heterozygous
1 Homozygous Dominant, 1 Heterozygous	All Dominant	2:0:2
1 Homozygous Recessive, 1 Heterozygous	1:1	0:2:2

Random Information:

- A person with blood type AB cannot produce children with blood type O. This is because that person has alleles I^A and I^B. However, to have children with blood group O has to have 2 I^o alleles, and this means that both parents have to have at least 1 I^o allele each
- Alleles that code for sex linked traits are recessive. Examples for sex linked traits:
    - Albinism
    - Sickle Cell Anaemia
    - Colour blindness
- Certain sex linked diseases come with their own benefits. For example, one with the sickle cell anaemia cannot have malaria as the malaria bacteria uses the red blood cells to their advantage. As such, if one were to be a heterozygous (have a sickle cell anaemia recessive allele), then the sickle cell anaemia disease would not be reflected in his phenotype, but he is still offered protection from malaria.
- For sex linked diseases (working with X and Y chromosomes), always use X and Y with superscripts for alleles!
- Sex linked traits are always on the X chromosome!

Carriers:

- As males have only 1 X chromosome, they are either affected by the sex linked disease (means their only X chromosome has a recessive allele for that sex linked disease) or they are unaffected by the sex linked disease (means their only X chromosome has a dominant allele).
- As females have 2 X chromosomes, to be affected by the disease, they would need to have both X chromosomes containing a recessive allele.
    - Unaffected (normal) – both X chromosomes have a dominant allele for the sex linked trait.
    - Carrier (normal, but still contains the allele for the disease) – 1 X chromosome has a dominant allele while 1 X chromosome has a recessive allele. Therefore, due to the presence of the dominant allele, the disease will not be present in the woman.

    - Affected – both X chromosomes contain recessive alleles for the gene responsible for the sex linked trait.
- That is why men are more prone to getting such sex linked traits, as compared to women.

Topic 3: DNA

General Notes

- Central Dogma: The main thesis of molecular inheritance.
    - It is a one-direction transfer from genetic information to proteins.
        - DNA replicates to produce more DNA
        - DNA undergoes transcription to produce mRNA
        - mRNA undergoes translation to produce polypeptide
- DNA stands for deoxyribonucleic acid, and is made up of many smaller subunits called nucleotides.
- Each nucleotide contains 3 different subunits:
    - A nitrogenous base (4 types present in DNA)
        - Guanine (which bonds with Cytosine)
        - Cytosine (which bonds with Guanine)
        - Adenine (which bonds with Thymine)
        - Thymine (which bonds with Adenine)
        - In RNA, the Thymine is replaced with Uracil (so A pairs with U, and U pairs with A)
    - A phosphate group
    - A sugar
- Different nucleotides of a single strand are bound together by covalent bonds between the sugar of one nucleotide, and the phosphate group of another, causing one long, single strand.
- The nitrogenous bases also bond with another with hydrogen bonds in a process called **complementary base pairing**.
    - Adenine with Thymine (double hydrogen bond)
    - Thymine with Adenine (double hydrogen bond)
    - Guanine with Cytosine (triple hydrogen bond)
    - Cytosine with Guanine (triple hydrogen bond)
    - This causes two strands to be bonded to one another by this complementary base pairing, therefore causing the double helix.
- DNA vs RNA:
    - DNA:
        - 4^{th} nitrogenous base is Thymine
        - Double Strand
        - Sugar is deoxyribose -hydrogen (H)
        - Comes as a double helix
    - RNA:
        - 4^{th} nitrogenous base is Uracil
        - Single Strand

        - Sugar is ribose -hydroxide (OH)
        - Comes as a single strand, or in a loop (usually hairpin)
- DNA & RNA Similarities:
    - Both contain a sugar-phosphate backbone
    - Both have 4 different types of nitrogenous bases
    - Both are involved in the synthesis of proteins
    - Both are nucleic acids

DNA Replication

Purpose: The purpose of DNA replication is to replicate the genetic information which will be sent to the daughter cell during mitosis. It is a way of copying DNA to produce new molecules with the same base sequence.

- An enzyme called helicase breaks the hydrogen bond between the bases, and the two individual strands (which are anti-parallel to one another) are unwound, producing two identical strands.
- Each single strand acts as a template for new strands. Free nucleotides that are present in large numbers in the nucleus, and the bases of these free nucleotides from new hydrogen bonds with the bases on each parent template strand, with help of the enzyme called DNA polymerase.
- As the template strands are identical, the sequence of bases on the 2^{nd} strand produced will be the same for both template strands.
- Each set of double stranded DNA now coils back up into a double helix.

Transcription and Translation

Purpose of Transcription and Translation: To reflect the genetic code in terms of a polypeptide chain (protein) in order to show the phenotype of a particular genetic code.

Genes to Polypeptides: Polypeptides are long chains of amino acids, and there are 20 different amino acids that can be arranged and repeated in any order to form a polypeptide. To make one particular polypeptide, amino acids must be linked up in a precise sequence. Genes store the information required for making polypeptides (in a coded form). From the coded information in a gene, transcription and translation occurs before it a polypeptide is produced.

The Genetic Code: The genetic code is a triplet code, with 3 bases corresponding to one amino acid. A group of three bases is called a codon, and three bases in a particular sequence (according to the universal genetic table) correspond to one amino acid, and a group of 3 bases is called a codon. As there are 64 codons and only 20 amino acids, the genetic code is degenerate (two or more codons code for the same amino acid). Also, the genetic code is universal – all organisms, including viruses, use this code.

Transcription

- The DNA double helix uncoils and the two strands are separated by RNA polymerase.
- Free RNA nucleotides are assembled, using one of the two DNA strands as the template, by RNA polymerase.

- The RNA nucleotides and are linked up to form a strand of RNA (also by RNA polymerase), by following complementary base pairing (only that adenine now pairs with uracil instead of thymine, as the nucleotides are RNA nucleotides).
    - Note that the RNA strand contains Uracil, wherever the template strand contained Adenine.
- The single strand of RNA (called mRNA) separates from the DNA.
- The double helix of the DNA strand is recoiled.

Translation

The strand of mRNA will then pass out of the nucleus, and into the cytoplasm. The DNA would have been unable to do so because it was in a double helix, whereas the mRNA, being in a single strand, is still small enough to travel out of the nuclear envelope.

- mRNA binds to the ribosome. It contains a series of codons (triplet bases) each of which codes for one amino acid.
- tRNA molecules are present around the ribosome in large numbers. Each tRNA has a special triplet of bases called an anticodon, and on the other end it carries the corresponding amino acid. Each anticodon contains three bases that are anti-parallel to the respective codon.
- The anticodon of the tRNA carrying the respective amino acids bind to the codon on the mRNA (which is on the ribosome) by complementary base pairing, therefore forming hydrogen bonds between the mRNA and the tRNA. This activates protein synthesis. Two tRNA bind to the mRNA at any one time.
- The two adjacent amino acids carried by the tRNA molecules are bonded together by a peptide linkage. The upper tRNA leaves the peptide chain with the lower tRNA, and detaches, and the ribosome moves along the mRNA to the next codon, and the tRNA that was earlier on the lower end now moves to the upper end, and another tRNA binds with it on the lower end, and the tRNA that is now at the upper end detaches, gradually forming a larger and larger polypeptide chain. These stages are repeated until the polypeptide is formed.

General Notes on Processes

- The tRNA is an RNA strand in a hairpin loop that is covalently bonded to an amino acid at one end, and at the other end, there is a sequence of three bases called an anticodon. These bases are complementary to the codon of mRNA that code for a specific amino acid.
- The non-template strand during transcription is also called the coding strand, or sense strand.
- To find out which codon codes which amino acid, we can refer to the universal genetic code.

Genetic Engineering

Restriction enzymes – Enzymes that cut DNA at specific sites.

DNA Ligase –After restriction enzymes cut DNA at specific sites, “sticky ends” will be formed, where part of the DNA is cut off from the rest of it. DNA ligase repairs these sticky ends by completing the DNA backbone by forming covalent bonds.

Vector – A DNA molecule used as a vehicle or carrier to transfer genetic material from one cell to another. Used a lot in genetic engineering.

Plasmid – Circular DNA that is often found in bacteria cells. They can alter the characteristic of the cells in which they are found, and are able to replicate independently.

Hence, restriction enzymes and DNA ligase can therefore be used to cut and paste different sequences of DNA from different sources, allowing scientists to do a great variety of genetic engineering.

Advantages of using bacteria to produce insulin (as compared to producing it by other methods):

- Bacteria is able to replicate at a very fast rate, resulting in high yield of insulin.
- Bacteria are small and easy to manipulate and cleaner to work with than animals.
- Insulin produced is identical to human insulin.

Disadvantages of extracting insulin from animals:

- Risk of patient developing immune responses to bovine or porcine insulin due to difference in chemical structure or contamination.
- Costly and time consuming (animal needs to be reared, and then sacrificed just for a mere amount of insulin)

Case study to produce human insulin:

1. Insulin gene is cut out from human DNA using restriction enzymes.
2. Plasmid is extracted from bacterium and same restriction enzyme is used to cut plasmid.
3. Human insulin gene is inserted into plasmid using DNA ligase creating a recombinant plasmid. The recombinant plasmid is then returned to the bacterium.
4. Bacterium reproduces quickly. New bacteria formed also carry the recombinant plasmid.

Appendixes

Appendix 1 – Assisted Reproductive Technologies

1. How can assisted reproductive technology help the following couples? Taking into account practical considerations like costs, risks and pros and cons, propose and describe a plan for each couple.

   a) Edward, 31 and Samantha, 30: Edward has no known fertility issues. Samantha has had a hysterectomy (removal of uterus) twelve years ago due to severe endometriosis, but she has ovaries which are able to manufacture healthy ova.

   The couple will need to engage a **gestational carrier**; Samantha can have her eggs extracted and fertilized by Edward's sperm as is done during a normal IVF (with or without ICSI) cycle. The embryo is then transferred into the uterus of the gestational carrier (instead of Samantha), who will carry the foetus for 9 months.

However, given that surrogacy is illegal in Singapore, they will likely have to engage a gestational carrier from another country. Additionally, they will also have to host and sponsor the gestational carrier to a significant extent.

b) Jason, 41 and Mabel 34: Jason is currently undergoing radiation treatment to treat his tumour in his stomach. As a result, his sperms are damaged, leading to low sperm count and quality. Mabel has no known fertility issues.

Depending on the severity of the damage to Jason's sperms, the couple has a few possible options:

1. **Artificial insemination** – If Jason's sperms are not very greatly damaged, his sperms can be washed and frozen from multiple ejaculations over a few weeks, before being concentrated and inseminated directly into the uterus.
2. **IVF with ICSI** – Jason's sperms can be screened until viable sperms are found, and then injected into an egg extracted from Mabel during a regular IVF. The fertilized embryo is then transferred into Mabel's uterus.
3. **Sperm donor, artificial insemination** – If Jason does not have any viable sperms, then the couple will have to resort to using a sperm donor or obtain viable sperms from a sperm bank. The donated sperm is inseminated into Mabel's cervix or uterus.

As IVF/ICSI is significantly more expensive to perform than artificial insemination, the couple may opt to try the latter before moving on to the former.

c) Thomas, 28 and Rachel, 28: Thomas has no known fertility issues. Both Rachel's Fallopian tubes are scarred and blocked due an infection two years ago, so although she has a healthy uterus and ovaries, her ova are unable to reach her uterus.

The couple can opt to do **IVF (with or without ICSI)**. Rachel's eggs are extracted and then allowed to be fertilized with Thomas' sperms. Fertilized eggs are cultured until they become an embryo, and then transferred back into Rachel's uterus.

2. Describe a scenario where artificial insemination is needed for a married couple which does not involve using sperms from a donor.

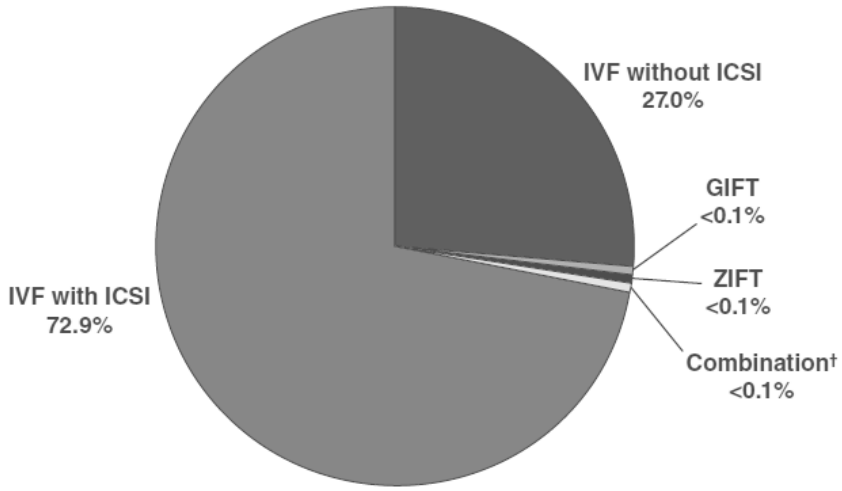
There are many possible scenarios. However, the common theme is that the woman has no fertility issues, and the man must be able to produce viable sperms:

- Erectile dysfunction or inability to ejaculate
- Premature ejaculation or inability to ejaculate in the woman's vagina
- Retrograde ejaculation
- Blocked vas deferens
- Sexual dysfunction; inability to engage in proper sexual intercourse due to painful intercourse or psychological issues etc
- Unusually hostile vagina environment (for sperms)

Class Discussion

3. The figure below shows the specific type of ART performed among women in the U.S. in 2009. 'GIFT' and 'ZIFT' (Gamete and Zygote IntraFallopian Transfer respectively) are variations of ART in which unfertilized gametes or fertilized embryos are transferred into a woman's Fallopian tubes. Artificial insemination is not covered in this study.

Figure 28
Types of ART Procedures Using Fresh Nondonor Eggs or Embryos,*† 2009



*Total does not equal 100% due to rounding.
† Combination of IVF with or without ICSI and either GIFT or ZIFT.

Taken from: Centers for Disease Control and Prevention, et al. *2009 Assisted Reproductive Technology Success Rates: National Summary and Fertility Clinic Reports*. Atlanta: U.S Department of Health and Human Services; 2011