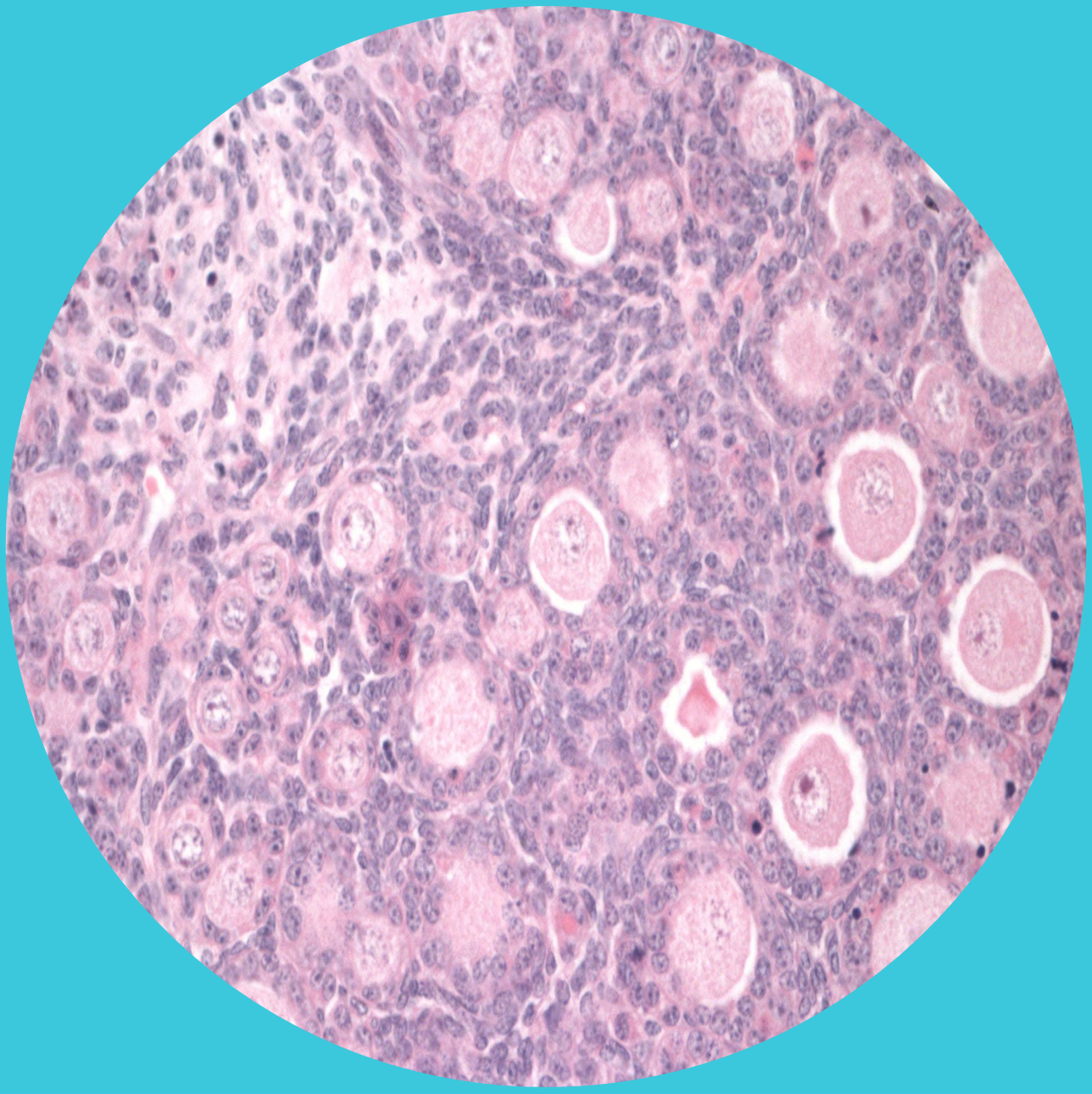
Researchers in Schools



How does chemotherapy damage the ovary?

Key Stage 4 Programme

Pupil Name

Coursebook Designed by Dr S Morgan

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Timetable and Assignment Submission

Timetable – Tutorials

Tutorial	Date	Time	Location
1			
2			
3			
4			
5			
6 (Feedback)			
7 (Feedback)			

Timetable – Homework Assignments

Homework Assignment	Description	Due Date
Tutorial 1		
Tutorial 2		
Tutorial 3		
Tutorial 4		
Tutorial 5		

Assignment Submission – Lateness and Plagiarism

Lateness	
Submission after midnight on 9th August	10 marks deducted
Plagiarism	
Some plagiarism	10 marks deducted
Moderate plagiarism	20 marks deducted
Extreme plagiarism	Automatic fail

Course Rationale

As survival rates for cancer patients increase, we need to start thinking about the long-term side effects of anti-cancer treatments. One of the main ways we treat cancer is with chemotherapy drugs, and these are commonly linked to problems with fertility (having children) in women after treatment. It is estimated that between 25-100% of young women who are treated with chemotherapy go on to have fertility problems. This can have a massive effect on their quality of life. Whilst we have known for a long time that chemotherapy can cause fertility problems in women, exactly how this happens isn't well understood. If we understand it, we may be able to stop it!

In this project, we will look at:

- How the ovary is structured and the different cells in it (using tissue sections and microscopes).
- What chemotherapy does to cancer cells and how cells die.
- Why some of the cells of the ovary might be vulnerable to chemotherapy and what that means for fertility.
- Some of the possible treatments we could use to protect the ovary.

This set of tutorials will be delivered in the style of university teaching. The final assignment will be similar to the kind of assignments you would receive at university and will be marked using a university-style grading system. This will give you valuable experience of what it would be like to progress into further education.

Uni Pathways Mark Scheme 2020 – science-based assignments

	Subject Knowledge	Critical Thinking	Written Communication
1st	The work shows a depth of knowledge and understanding of key concepts and scientific methods, through engaging with relevant sources. Knowledge is used to build and support highly effective scientific arguments and explanations.	Analyses key scientific evidence, arguments, and reasoning. Interprets meaning and makes connections. Identifies and critically evaluates key scientific arguments and evidence, deciding on their credibility, strength, and relative significance, drawing convincing conclusions.	The work has a coherent flow and is well structured. The writing style is appropriate; scientific language and key scientific terms are used accurately and effectively to support the arguments and explanations made. There are no, or very few, errors in spelling or grammar. Consistent referencing, appropriate paragraphing and use of correctly labelled tables and graphs matching the style taught in the course.
2:1	The work shows an understanding of key concepts and scientific methods, drawing on relevant sources. Knowledge is used to build and support effective scientific arguments and explanations.	Analyses relevant scientific evidence, arguments, and reasoning. Identifies and critically evaluates relevant scientific arguments and evidence, deciding on their credibility and strength, drawing reasonable conclusions. Shows some understanding of the relative value of evidence and arguments.	The work is well-structured. The writing style is appropriate; scientific language and key terms are used correctly. There are few errors in spelling or grammar. Mostly consistent referencing and use of tables and figures; matching the style taught in the course.
2:2	The work shows an understanding of key concepts and scientific methods, with no major misconceptions. Beginning to apply this knowledge to build and support effective scientific arguments and explanations.	Identifies and uses basic scientific evidence, arguments, and reasoning. Showing some understanding of the quality of scientific arguments and evidence. Not yet showing understanding of the relative value of evidence and arguments.	The work has some structure. The writing style can sometimes be informal; occasionally scientific language and key terms are not used when it would be appropriate to do so. There are some errors in grammar and spelling do not get in the way of communicating the content. Referencing has some consistency; matching the style taught in the course Limited use of tables and graphs.
3rd	Shows a developing understanding of key concepts and scientific methods, with some misconceptions.	Beginning to analyse scientific evidence, arguments, and reasoning.	The grammar, spelling, style, and structure of the work need improving in order

	Does not yet apply this knowledge to build and support scientific arguments and explanations.	Describes evidence and arguments, while not yet evaluating them.	to communicate ideas to the reader. Scientific language, key terms and references are not always used correctly. Limited, or no use of tables and graphs.

Baseline Assignment (essay based): Pupil Feedback Report

Name of Pupil	
Name of School	
Name of RIS teacher	
Title of Assignment	

How your assignment is graded:

Grade	Marks	What this means
1st	70+	Performing to an excellent standard at A-level
2:1	60-69	Performing to a good standard at A-level
2:2	50-59	Performing to an excellent standard at GCSE
3rd	40-49	Performing to a good standard at GCSE
Working towards a pass	0-39	Performing below a good standard at GCSE
Did not submit	DNS	No assignment received by The Brilliant Club

Lateness	
Any lateness	10 marks deducted
Plagiarism	
Some plagiarism	10 marks deducted
Moderate plagiarism	20 marks deducted
Extreme plagiarism	Automatic fail

Marks

OVERALL MARK / 100		FINAL MARK / 100 (including any deductions)	
DEDUCTED MARKS		FINAL GRADE	

If marks have been deducted (e.g. late submission, plagiarism) the teacher should give an explanation in this section:

Mark Breakdown and Feedback

Subject knowledge	
	mark
Critical thinking	
	mark
Written communication	
	mark

Subject Vocabulary

Word	Definition	In a sentence
Fertility	The ability to have children/produce young.	The doctor ordered a fertillity test for her patient.
Gamete	One of the cells that join together to begin making a baby. Also called germ cells or sex cells.	In females, the gametes are called eggs and are stored in the ovary.
Egg	Female gamete which is produced and stored in the ovary and combines with sperm during reproduction to produce a baby. Can also be called an oocyte or ovum.	The egg is released from the ovary.
Sperm	Male gamete which combines with the egg during reproduction to produce a baby.	The sperm fertilised the egg.
Fertilisation	When two gametes (egg and sperm) join together.	Fertilisation is when a single sperm fuses with an egg.
Ovary	Organ(s) in women and female animals that produce eggs and female hormones.	After an egg is released from the ovary, fertilisation can occur.
Ovulation	To release an egg from the ovary so it can combine with a sperm cell.	Ovulation occurs once a month.
Menopause	The time in a woman's life when she runs out of eggs in her ovaries (less than 1000 left). Usually happens around the age of 51.	She is going through the menopause.

Launch Event

The launch event is your opportunity to learn more about this course and Uni Pathways. You will watch some videos, listen to your teacher and have some discussion. Below is some room to make notes for some of the videos you will watch during the event.

Virtual Campus Tours

Notes…

The Scholars Programme Alumni

Notes…

Student Ambassadors

Notes…

Tutorial 1 – What is Fertility?

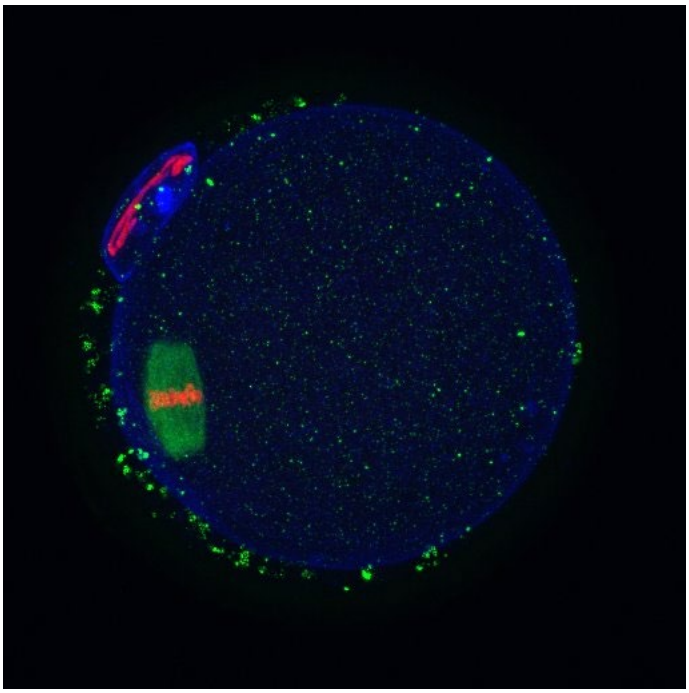


Fig 1. An egg cell which has been stained and imaged using a microscope. DNA is stained red, the cell membrane is blue and the green shows microtubules.

What is the Purpose of Tutorial 1?

This tutorial will focus on introducing the idea of female fertility; how we can measure it and how we define it. It will also introduce the idea of its limitations and how drugs such as chemotherapy can affect it.

By the end of the tutorial, you should be able to:

1. Describe how we measure and define fertility
2. Explain the concept of the menopause and Premature Ovarian Insufficiency

Activity 1. What is the definition of fertility?

Fertility is the ability of a person to have children. Being able to produce a baby relies on two different cell types: the egg and the sperm (these cells are called gametes).

There are many factors that fertility could depend on but the main one we are interested in for this course is the number of eggs in the ovary. What are some other problems that can happen in women that cause fertility problems? Write down ideas in the space below:

Fill in the gaps in the sentences below:

The eggs are stored in an organ called the ……. They are released from the ovary in a process called …….. This means they can meet…….. in the fallopian tubes in a process called ……

How are eggs different to the other cells of the body? Write down ideas in the space below

Activity 2. Egg loss and the menopause

Look at the graph below. It shows the number of eggs in the ovaries of average women (here they use the word follicle instead of egg- we will cover why that is next week!). The numbers on the y axis might seem a bit strange- that is because they have been written in a logarithmic scale as they cover a very big range and this scale makes it easier to understand. The little number shows how many times you multiply 10 by itself (e.g. 10^2 is 10 x 10= 100). The line is a line of best fit so it shows the average.

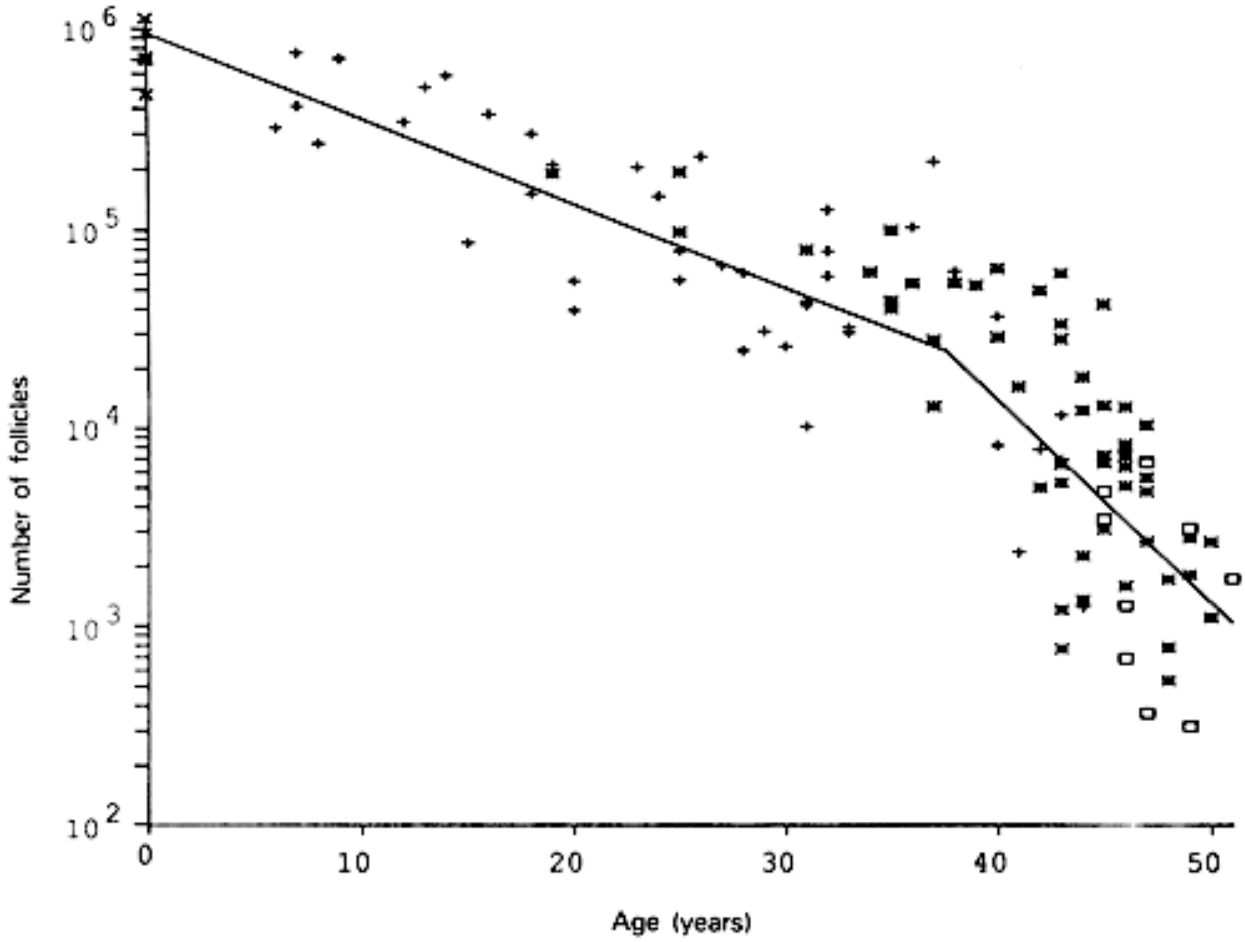


Fig 2. The age related decrease of eggs in women (Faddy et al, 1992)

Look at the graph and answer the following questions:

1) How many eggs does the average women have at birth?

2) What age does the number of eggs start to fall more quickly?

3) When is the menopause and how many eggs are left at that point?

4) How do you think something toxic like chemotherapy could change this graph? What is this called?

Tutorial Glossary

Write down any new words you would like to remember in the table below

Word	Definition	In a sentence

Notes

References

Faddy MJ, Gosden RG, Gougeon A et al: Accelerated disappearance of ovarian follicles in mid-life: Implications for forecasting menopause. Hum Reprod 7:1342, 1992.

Homework: Baseline assignment

What are eggs and how are they important for female fertility?

1. Draw a simple diagram of an animal cell. Identify the different organelles in the cell and create a table identifying the main function of each of these.

2. Where in the reproductive tract are the eggs/gametes located?

3. What do you understand by the word gamete? How are they different from the rest of the (somatic) cells in your body?

4. Can a women ever run out of gametes (eggs)? Why? What is it called when this happens? (100 words)

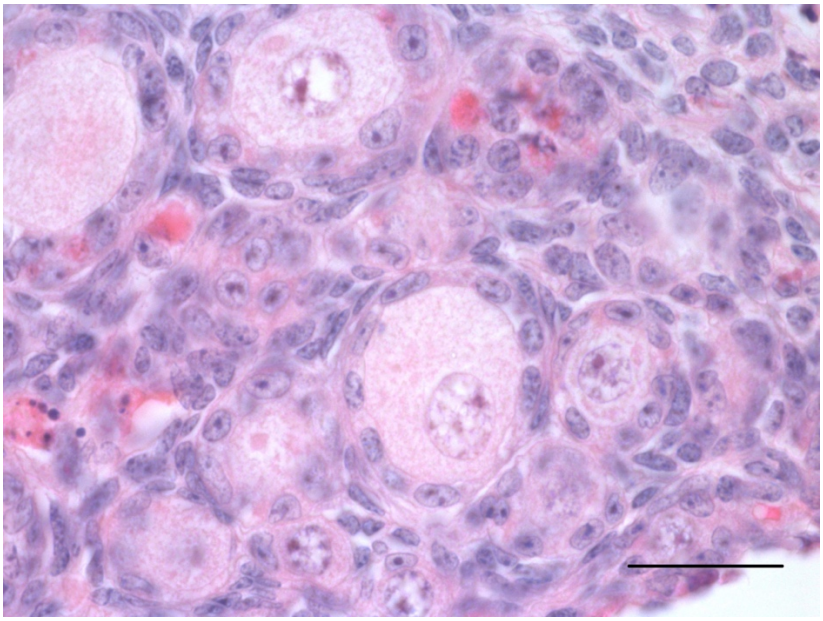
5. What is cancer and how is it treated? What are common side effects of using these kind of treatments? (100 words)

Success criteria – how to structure your assignment and what to include:

- Please use full sentences and paragraphs when appropriate. Don't use bullet points.
- Use accurate spelling, grammar and punctuation.
- Research from outside sources if you need to but reference them correctly if you do

Organelle	*Function*

Tutorial 2 – How is the ovary organised?



What is the Purpose of Tutorial 2?

This tutorial will focus on the structure of the ovary and the way the different cells are organised. To do this, we will be looking at microscope slides of sections of mouse ovaries and identifying the key structures.

By the end of the tutorial, you should be able to:

1. Describe the different cell types of the ovary and how they are organised
2. Explain the difference between a germ cell and a somatic cell
3. Describe the structure of an ovarian follicle and the different stages of folliculogenesis

Activity 1: Using a microscope to look at sections

Today you will be looking at sections of mouse ovaries down a microscope. This means that a mouse ovary was preserved, sliced very, very finely and put onto a slide so that we can see the structure to a one cell thickness (too thick and it becomes difficult to see each cell on its own!). It has been stained with two dyes: haematoxylin and eosin. Haematoxylin is a purple stain and dyes the nuclear material (DNA). Eosin is a pink dye which stains the cytoplasm.

There are two main cell types in the ovary: the eggs (called the gametes/germ cells/oocytes) and the somatic cells. The eggs are the largest cells of the body and will be more obvious down a microscope as they have more cytoplasm than the somatic cells. This means they look a bit like pink bubbles.

Set up microscope

Rotate the objectives so that low power objective lens is in line with the stage.

Turn the coarse focus to adjust the space between the stage and the objective lens.

Carefully place the slide on the microscope so the cover slip is facing up.

Line it up so the specimen is in the centre of the stage where the light passes through.

Focus the slide using the fine focus. You can then move up through the higher objectives by rotating the objective lenses to see cells more clearly. You will need to refocus as you change between lenses using the fine focus.

Look at your slide and answer the following questions:

1. Can you see eggs of different sizes in your tissue section? Why do you think that is?

2. What do you think the small circle in the centre of the egg is?

3. Look at the cells around the egg? Are they organised in any kind of structure? How would you describe it?

4. What are 2 major differences between eggs and the rest of the cells in your body?

Activity 2: What is folliculogenesis?

The structure that the eggs are found in is called a follicle. This consists of an egg surrounded by some somatic cells (called granulosa cells). The resting population (most of the eggs) are contained in a primordial follicle (an oocyte/egg surrounded by a few flattened granulosa cells). These are the hardest to spot in a section as they are the smallest. Can you see any?

Follicles are activated to grow and will then go through various stages of growth and development before reaching the preovulatory phase and being ovulated (or dying as most eggs do). Below is a cartoon of some of the different phases of egg development (a process called folliculogenesis). Can you spot any of them on your sections? Write down the stages that you can see

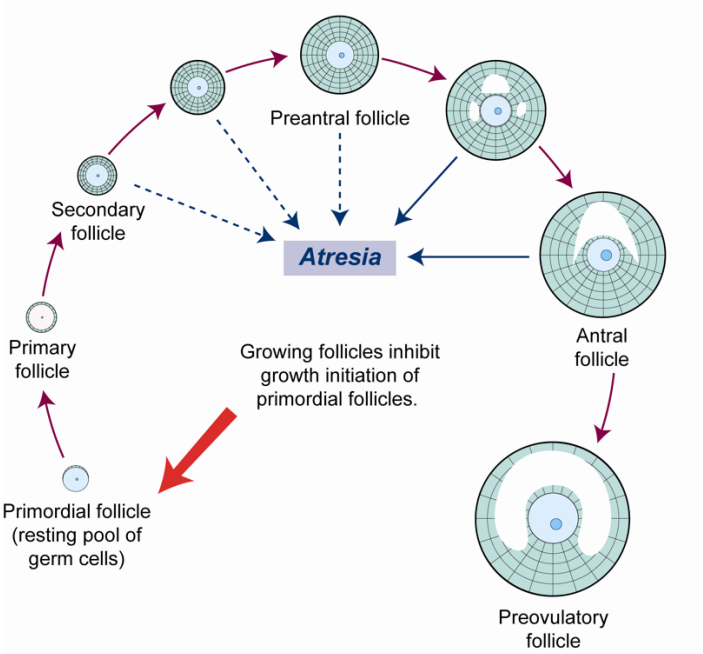
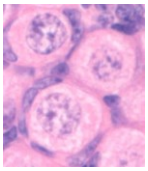
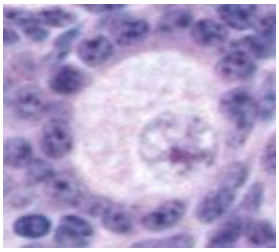


Fig 1. Diagram showing the process of folliculogenesis. At any one time, a small cohort of primordial follicles are recruited out of the resting pool and activated to grow. Of the follicles that are activated, only one will make it to the preovulatory stage and be ovulated; the others will die from follicle atresia (atresia is another fancy word for cell death). Although the majority of follicles which are lost from atresia are from the antral stage (indicated by the solid lines), follicles can be lost from any stage of folliculogenesis (indicated by the dashed lines). Adapted from Morgan *et al*, 2012.

Label the two diagrams below. What stage of follicle is each and how can you tell?





Homework

Think about and write answers to the following questions. If you need to, do some extra research (remember to write your references):

How long can a primordial follicle last/be stored in the ovary before its activated to grow?

How long does folliculogenesis take in humans?

Why do you think eggs have so much more cytoplasm than other cells?

Tutorial 3 – How do cells die?

What is the Purpose of Tutorial 3?

This tutorial will cover one of the main processes by which cells die (apoptosis) and its role in the ovary

By the end of this tutorial, you should be able to:

1. Explain the concept and mechanism of programmed cell death (apoptosis)
2. Discuss the different cell types of the ovary and when they normally undergo cell death

Activity 1. Cell death

Cells die all the time. It is an important process for

1. Growth and development
2. Tissue homeostasis (e.g. keeping an organ the right size)
3. Response to injury, infection or something toxic

There are several different ways that cells can die. Write the definitions down for each of the following:

APOPTOSIS:
……
……
……

NECROSIS:
……
……
……

AUTOPHAGY:
……
……
……

When cells die through apoptosis, they go through several key stages. Put these stages in order that they happen:

Macrophage (cell from immune system) recruitment

Organelle disintegration

Membrane blebbing

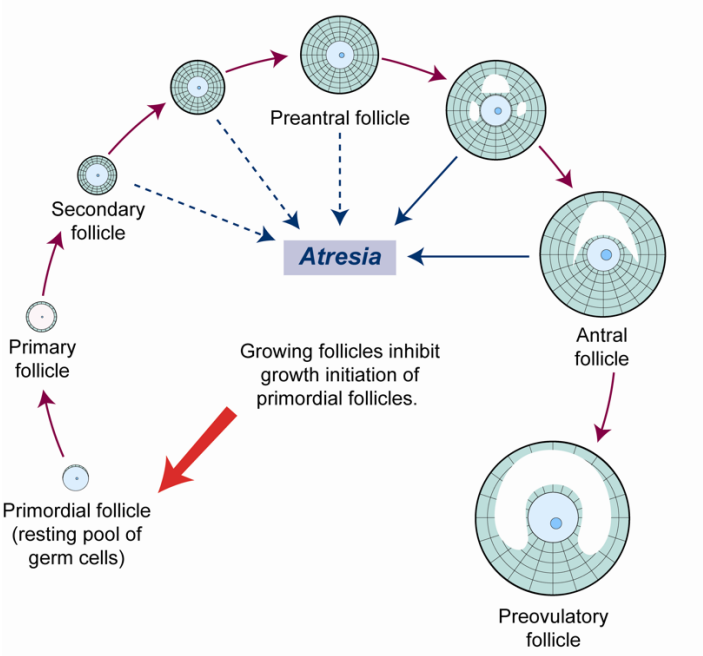
Cell shrinkage

Chromatin (DNA) condensation

Do you think that you could tell if a cell was dying from apoptosis looking at it on section (like we did last week)? How might it look?

Activity 2. Cell death in the ovary

Look at the diagram of folliculogenesis that we discussed last week:



Atresia is a fancy word for follicle death through apoptosis. If you look at the diagram, the solid lines show that the biggest stages of follicle is more likely to die. Why do you think this is?

On the diagram, it doesn't look like early follicles die. Do you think that they can? Why?

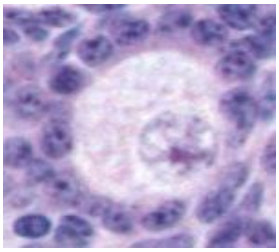
Homework

Think about and write answers to the following questions. If you need to, do some extra research (remember to write your references):

Think back to the graph in Tutorial 1. What happens to the number of the eggs in the ovary? Which two processes are important for this?

Why do you think most of the eggs in the ovary die?

Look at the structure of a follicle:



If the somatic (granulosa) cells around the egg die, what will happen to the egg? Why?

Tutorial 4 – Chemotherapy and the ovary

Photo by Michał Parzuchowski on Unsplash

What is the Purpose of Tutorial 4?

In this tutorial, we will cover how chemotherapy is used to treat patients and the effect it can have on the ovary. To do this, we will compare two different chemotherapy drugs (cisplatin and doxorubicin) and how they damage the ovary.

By the end of the tutorial, you should be able to:

1. Describe how and why chemotherapy is used to treat cancer patients

2. Pupils can compare two chemotherapy drugs: cisplatin and doxorubicin and their effect on the ovary

Activity 1. Cancer and chemotherapy

Answer the following questions

What is cancer?

How do we treat cancer aside from chemotherapy?

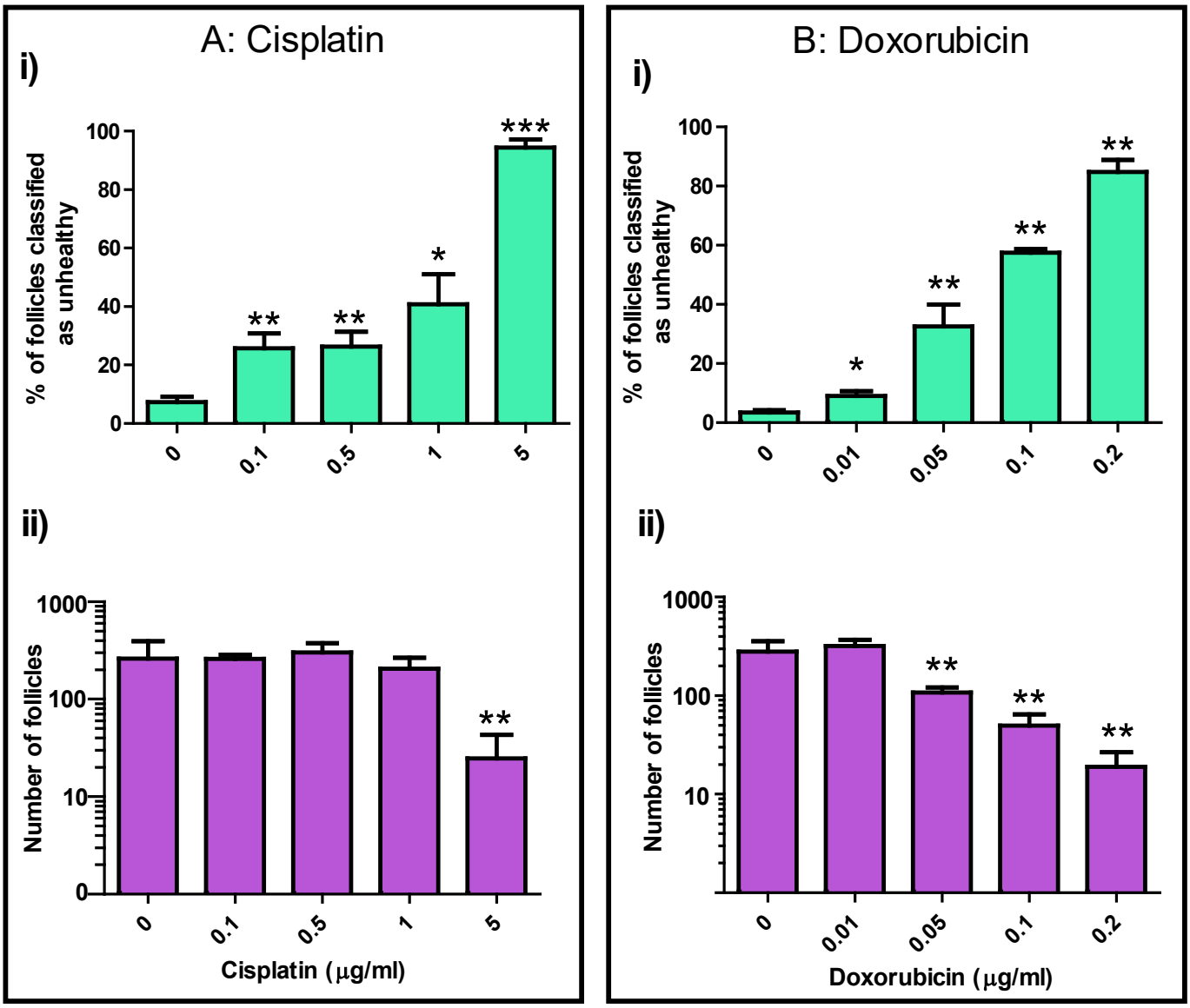
Is chemotherapy only given as a cancer treatment?

	Cisplatin	Doxorubicin
What kind of drug?		
What cancer is it used to treat?		
Main mechanism of action?		
Is it toxic to the ovary?		

Why do you think I chose these two drugs to study?

Activity 2. Cisplatin and Doxorubicin on the ovary

Thinking back to when we looked at ovarian sections under the microscope:
how can we tell if these drugs damage the ovary by looking at tissue sections?



Look at the graphs above. What do they tell you about the health and the number of ovarian follicles after treatment with cisplatin and doxorubicin?

Homework

Think about and write answers to the following questions. If you need to, do some extra research (remember to write your references):

What do you think are potential problems with using histology (the appearance of cells) to decide if a drug is toxic or not? What could we do to improve this experiment?

What difficulties do you think could exist in studying fertility like this? For example, is this kind of thing easy to look at humans? Can you think of any ways we can get around these?

Tutorial 5 – Can we stop the damage?

What is the Purpose of Tutorial 5?

In this tutorial, we will cover possible ways that we can prevent the damage that chemotherapy causes to the ovary.

By the end of the tutorial, you should be able to:

1. Consider different methods through which the ovary could be protected from damage during chemotherapy treatment
2. Evaluate the advantages and disadvantages of these methods

Activity 1. Cryopreservation

There are currently no approved treatments that are being used in clinics to protect the ovary during chemotherapy treatment. However, scientists have tried a few strategies out which we will talk about today!

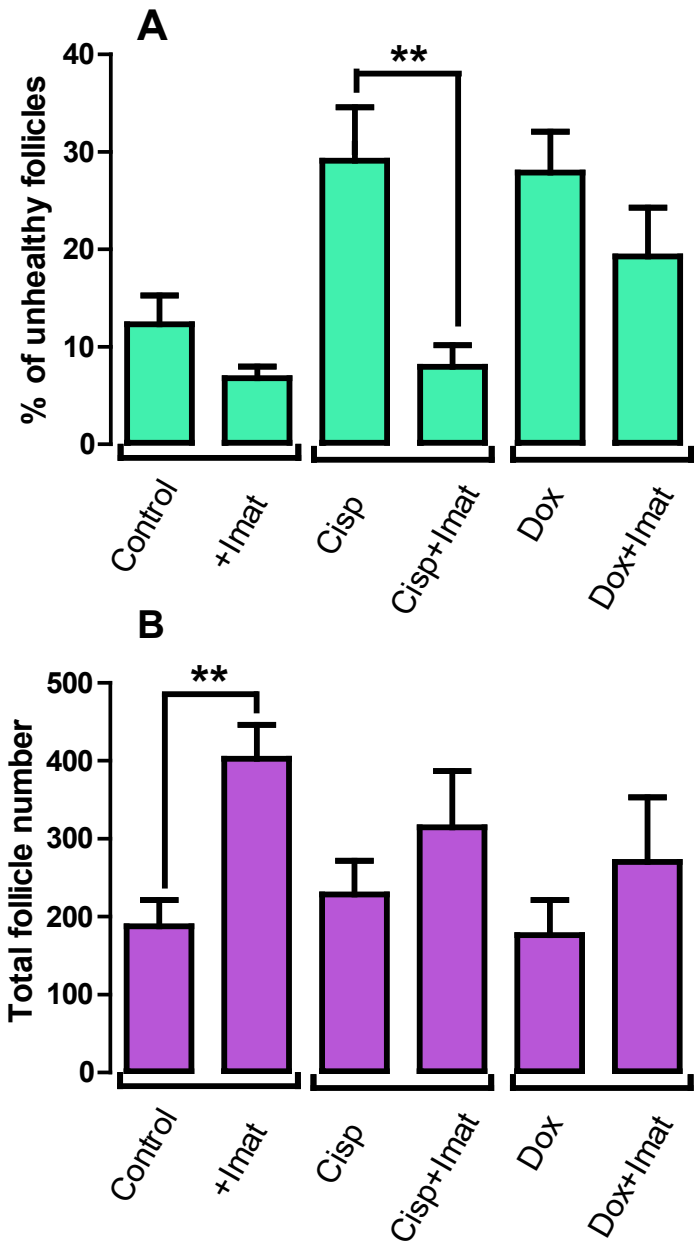
What is cryopreservation?

Fill in the table below. Which reproductive tissue/cells can we cryopreserve and what are some of the advantages and disadvantages we need to consider when doing this?

Tissue type	Advantage	Disadvantage

Activity 2: Imatinib as a possible treatment

One possible treatment is called imatinib (Gleevac). How does imatinib work in cells?



Look at the graphs above. Do you think imatinib will protect the ovary against all drugs? What do you think that might mean for patients on combinations of treatments?

Final Assignment: Discuss how chemotherapy drugs damage the ovary

Write a 2000 word essay discussing how chemotherapy drugs can damage the ovary, why different cell types might be more vulnerable than others and why it is important that we understand this treatment side-effect.

Success criteria – how to structure your assignment and what to include:

In your essay, please include:

- Compare the different cell types of the ovary. How are these cells normally arranged in the ovary?
- What is the difference between a gamete (oocyte/egg) and a somatic cell and why might that be important?
- Compare the chemotherapy drugs cisplatin and doxorubicin. How do they act on cancer cells and why might the cells of the ovary be vulnerable to them?
- Consider why understanding this side-effect of cancer treatment is important. Is there a way we can protect the ovary from damage during treatment?

Please structure your essay using subheadings including introduction and conclusion. Include diagrams or tables if they help you explain a point. These must be labelled and referred to in the text. References must be in the Harvard style (Author name, Year) or using a numbering system.

Tutorial 6 – Feedback tutorial

What is the Purpose of Tutorial 6?

- To receive feedback on your final assignment
- To respond to the feedback from your Uni Pathways teacher
- To write targets for improvement on your final assignment

Final assignment feedback from your Uni Pathways Teacher

(Remember to look at the mark scheme to help you understand what you have done well so far, and how you can do even better in your final assignment)

Here are three things that my Uni Pathways Teacher thought I did well in my draft assignment
•   •   •

Here are three things that my Uni Pathways Teacher thinks that I could do to get a higher mark in my final assignment
•   •   •

Tasks from my Uni Pathways Teacher to do during the feedback tutorial to help me improve
•   •   •
My response:

Actions I will take to improve my final assignment after this tutorial…
•   •   •

Hand in date for my final assignment:	

Tutorial 7 – Final tutorial

What is the Purpose of Tutorial 7?

- To receive feedback and a grade on your final assignment.
- To reflect on the programme including what you enjoyed and what was challenging.
- To ask any questions you may have about university.

Final assignment feedback from my Uni Pathways Teacher

Final mark:	University style grade:
Feedback: Here are three things that my Uni Pathways teacher thought I did well in my final assignment • • •	

Here are three things that my Uni Pathways teacher thinks I should remember for when I am doing this kind of study in the future
• • •

University

What questions do you still have about University after taking part in Uni Pathways?
• • •

Reflecting on Uni Pathways

What did you most enjoy about Uni Pathways?
• • •

What did you find challenging about the programme?	How did you overcome these challenges?
• • •	• • •

Appendix 1 – Referencing correctly

When you get to university, you will need to include references in the assignments that you write, so we would like you to start getting into the habit of referencing in your Brilliant Club assignment. This is really important, because it will help you to avoid plagiarism. Plagiarism is when you take someone else's work or ideas and pass them off as your own. Whether plagiarism is deliberate or accidental, the consequences can be severe. In order to avoid losing marks in your final assignment, or even failing, you must be careful to reference your sources correctly.

What is a reference?

A reference is just a note in your assignment which says if you have referred to or been influenced by another source such as book, website or article. For example, if you use the internet to research a particular subject, and you want to include a specific piece of information from this website, you will need to reference it.

Why should I reference?

Referencing is important in your work for the following reasons:

- It gives credit to the authors of any sources you have referred to or been influenced by.
- It supports the arguments you make in your assignments.
- It demonstrates the variety of sources you have used.
- It helps to prevent you losing marks, or failing, due to plagiarism.

When should you use a reference?

You should use a reference when you:

- Quote directly from another source.
- Summarise or rephrase another piece of work.
- Include a specific statistic or fact from a source.

How do I reference?

There are a number of different ways of referencing, and these often vary depending on what subject you are studying. The most important to thing is to be consistent. This means that you need to stick to the same system throughout your whole assignment. Here is a basic system of referencing that you can use, which consists of the following two parts:

1. **A marker in your assignment**: After you have used a reference in your assignment (you have read something and included it in your work as a quote, or re-written it your own words) you should mark this is in your text with a number, e.g. [1]. The next time you use a reference you should use the next number, e.g. [2].
2. **Bibliography**: This is just a list of the references you have used in your assignment. In the bibliography, you list your references by the numbers you have used, and include as much information as you have about the reference. The list below gives what should be included for different sources.

    a. **Websites** – Author (if possible), title of the web page, website address, [date you accessed it, in square brackets].

    E.g. Dan Snow, 'How did so many soldiers survive the trenches?', http://www.bbc.co.uk/guides/z3kgjxs#zg2dtfr [11 July 2014].

    b. **Books** – Author, date published, title of book (in italics), pages where the information came from.

    E.g. S. Dubner and S. Levitt, (2006) *Freakonomics*, 7-9.

    c. **Articles** – Author, 'title of the article' (with quotation marks), *where the article comes from* (newspaper, journal etc.), date of the article.

    E.g. Maev Kennedy, 'The lights to go out across the UK to mark First World War's centenary', Guardian, 10 July 2014.

Notes

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