

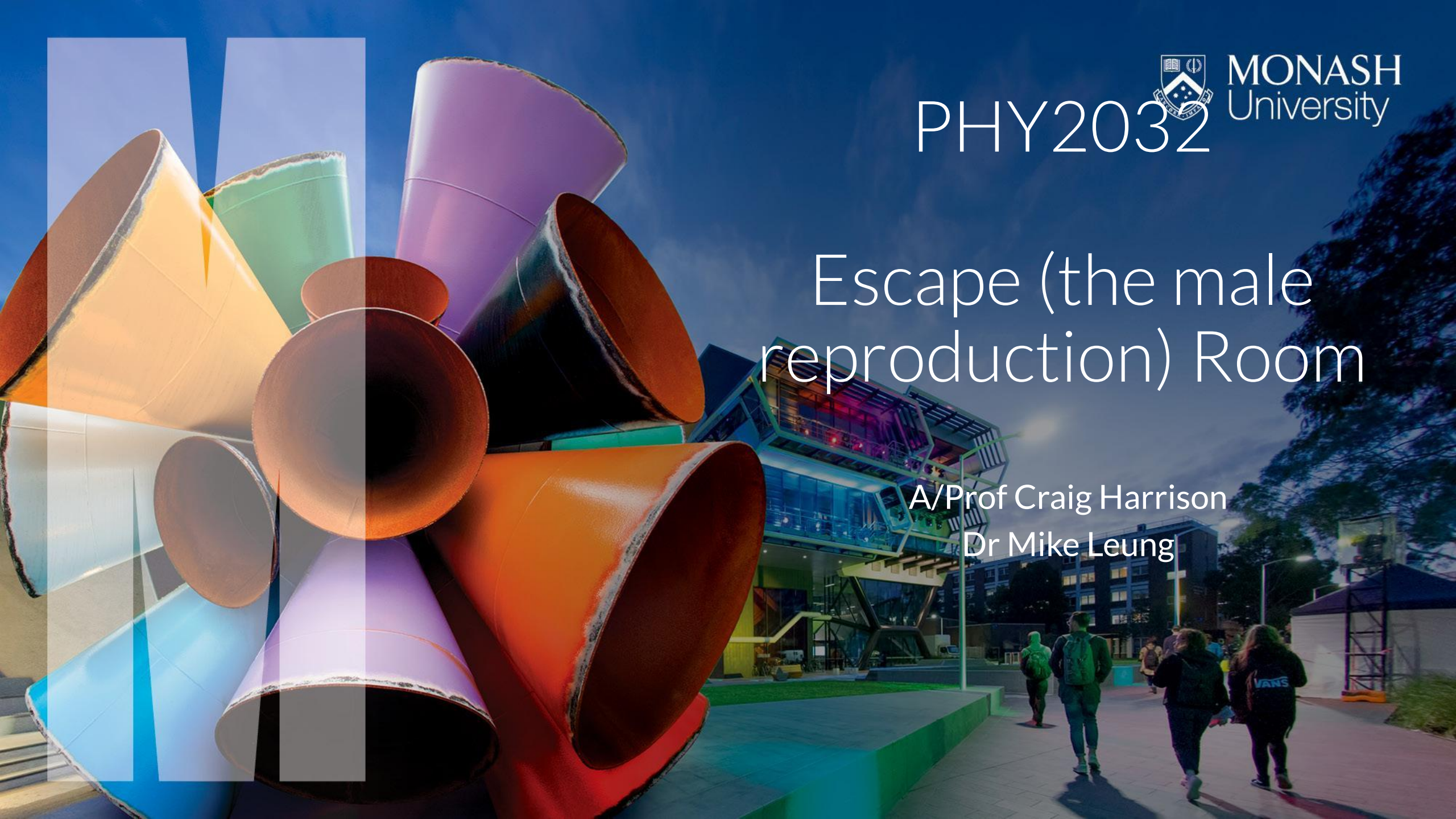


MONASH  
University

PHY2032

# Escape (the male reproduction) Room

A/Prof Craig Harrison  
Dr Mike Leung



# THE KING'S PROBLEM



# Notes from King Mikhail's Vlog

	King Mikhail says:
Video 1	
Video 2	
Video 3	
Video 4	
Video 5	
Video 6	

# ESCAPE ROOM - RULES

1. Each group selects a Head Scholar
2. Head Scholars from all groups assemble in the Apothecary to collect activity 1
3. Wait until all Head Scholars have the activity, then return to tables. For most activities there are 2 copies, so everyone can assist in solving the puzzle (please, only write on one copy).
  - 4a. Once you have determined the numerical/alphabetical code to unlock one of the Royal Vlogs, raise your hands
  - 4b. A Herald will swiftly (but safely) move to your table to confirm your answer and record your time (NB: You must show the Herald the completed activity + the code, i.e., you can't just guess the answer).
  - 4c. Wait patiently or heckle the teams around you who have yet to solve the puzzle
5. Time allowed for each activity will typically be 8-12 minutes. Groups that do not complete the activity will have the final stop-watch time entered in their records.
6. Everyone will watch the Royal Vlog entry and take note of the revealed medical history.
7. Head Scholars return to the Apothecary to receive the next activity etc.



# HEAD SCHOLARS – GATHER AT THE APOTHECARY





<https://www.timeanddate.com/stopwatch/>

## ACTIVITY 1a

- The processes involved in the development of the reproductive system are listed
- Unfortunately, they are encrypted
- Once fully deciphered, raise your hand and a herald will bring you Activity 1b

1.  
EΛJFΓOV KOΛOETE ΓO >NO JUVOΘLO E  
C J < ΛNFEBEVEBO

2.  
>OV>EV>OFEOO V>ΓB<EJ>OV B><FJ>ΓE  
O EC VELECCΓJΘ B<L>V

3.  
ΓEΘJBJE FΓBΓO LJΘ UOLEBO >OV>ΓV E  
F EΛJF<

4.  
ΘE JN JEEVV >NO B<LEOFΓJΘ B<L>V >  
E KOΛOETE

5.  
ΘE >OV>EV>OFEOO OOV<FOV >NO VELECCΓJ  
O B<L>V KOΓOΘOFJ>O

6.  
JN ΓOJ<LOV KOΓOΘOFJ>ΓEO EC B<LEOFΓ  
JΘ B<L>V

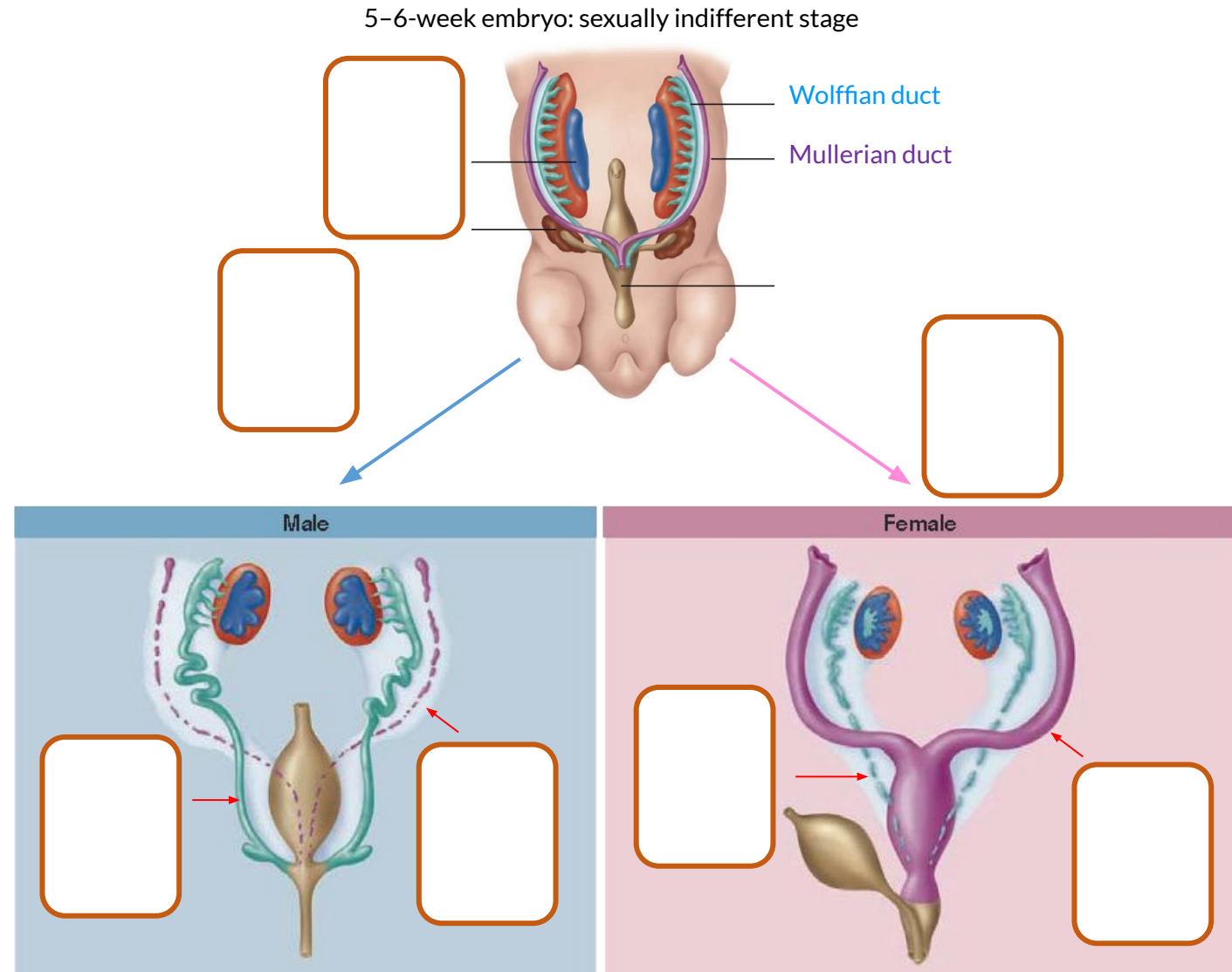
7.  
>OV>OV KOΛOETE ΓO >NO ΓFOVΘOLO E  
C J < ΛNFEBEVEBO

# ACTIVITY 1b

- From the deciphered list, add the step numbers to their correct spaces on this image of embryonic sex differentiation

- Raise your hands when you have the 7-digit code to unlock King Mikhail's first vlog entry

## SEX DIFFERENTIATION



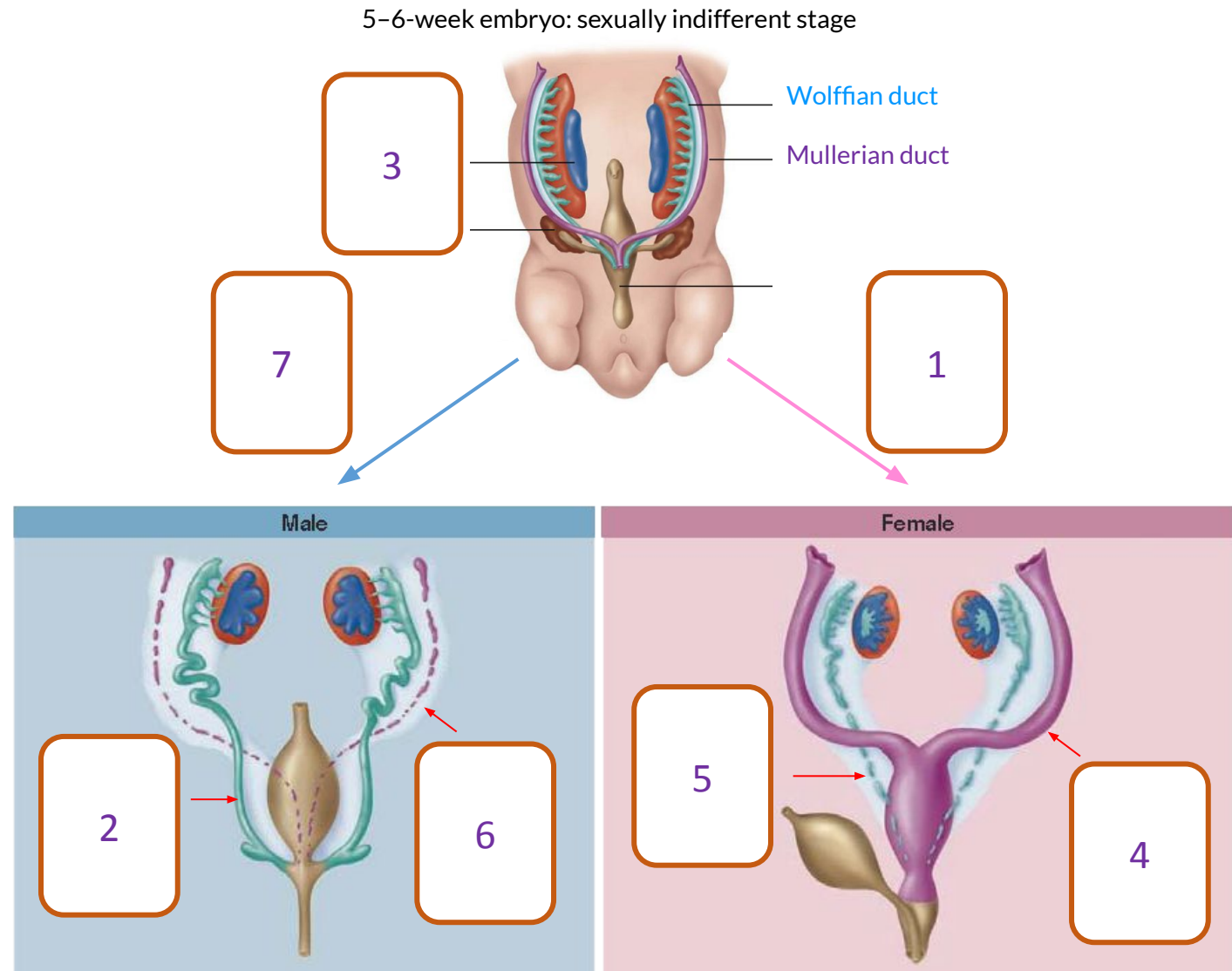
# ACTIVITY 1b

- From the deciphered list, add the step numbers to their correct spaces on this image of embryonic sex differentiation

- Raise your hands when you have the 7-digit code to unlock King Mikhail's first vlog entry

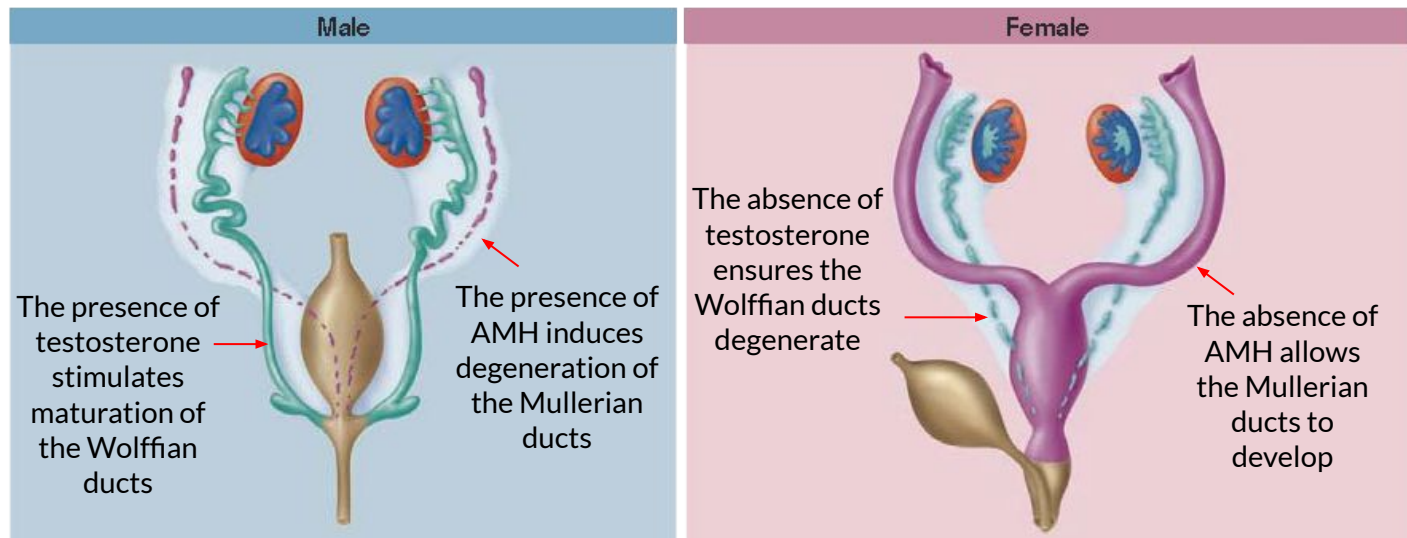
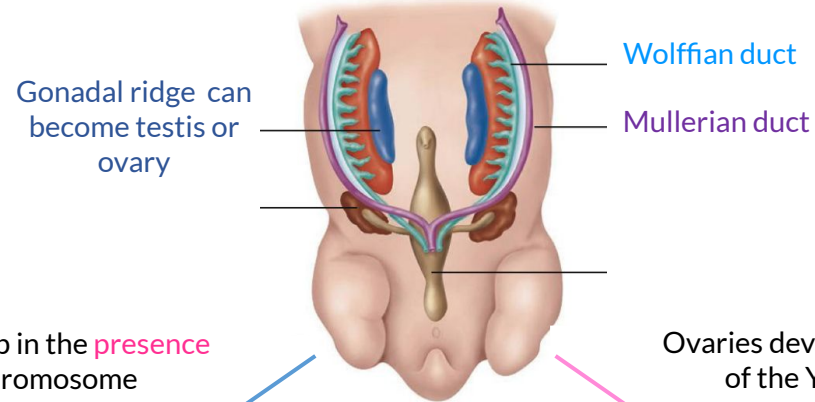
3 7 1 2 6 5 4

## SEX DIFFERENTIATION



# SEX DIFFERENTIATION

5-6-week embryo: sexually indifferent stage



# Vlog entry 1



# HEAD SCHOLARS – GATHER AT THE APOTHECARY





<https://www.timeanddate.com/stopwatch/>

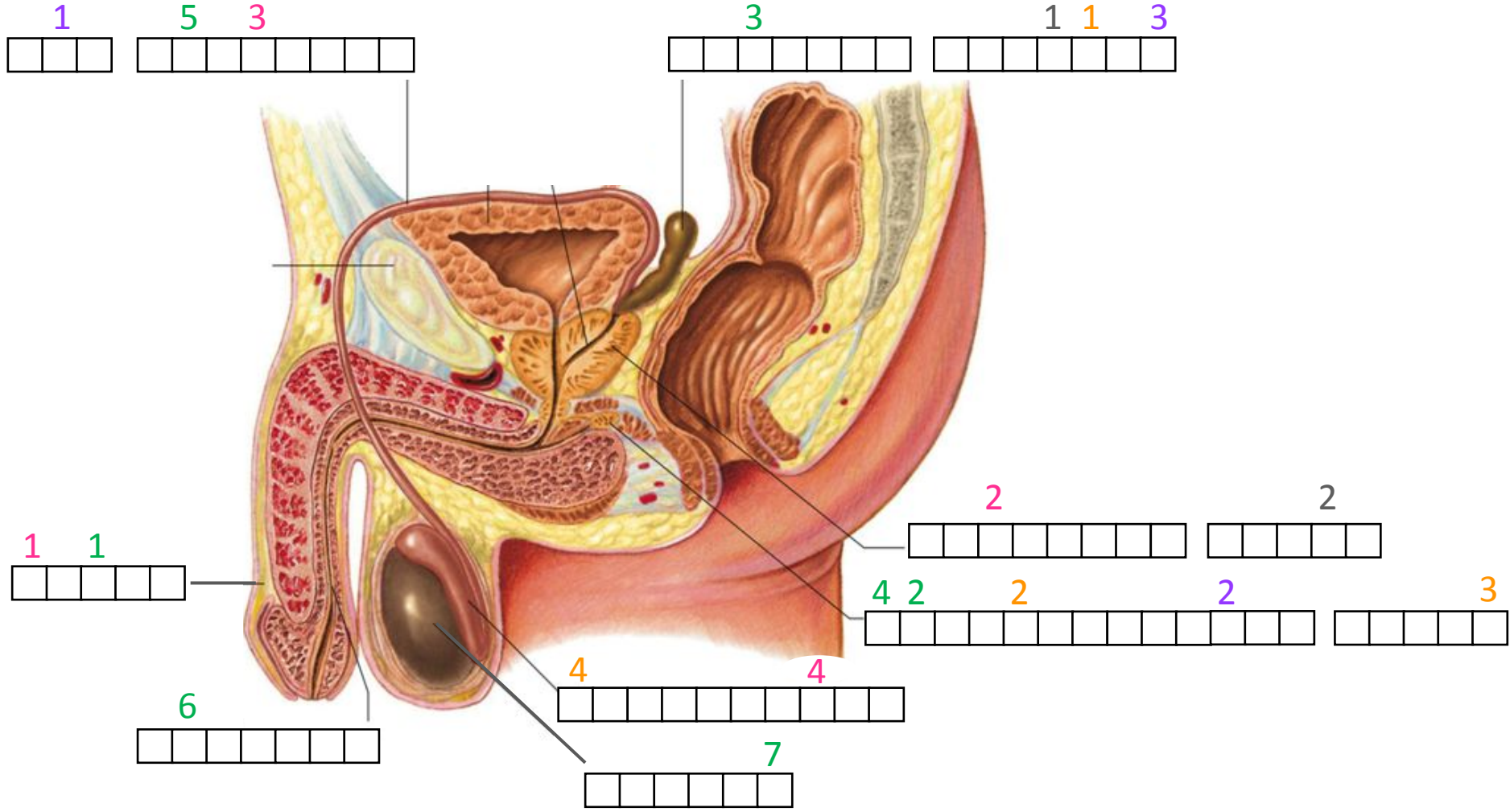
# ACTIVITY 2a

Label the male reproductive system

Answer Activity 2a before you attempt to solve Activity 2b

Memorise, then burn this parchment

(Disclaimer: This is just included for dramatic effect - please don't set fire to anything!)



# ACTIVITY 2b

## Anatomy Poem

By Chamberlain Craigos



Scrotum is one sac of skin that hangs outside the body  
Parked within (this sac of skin) two organs known as testes  
Oh, why did evolution create a system quite so shoddy  
Now cremaster and dartos muscles must contract when it doth freeze

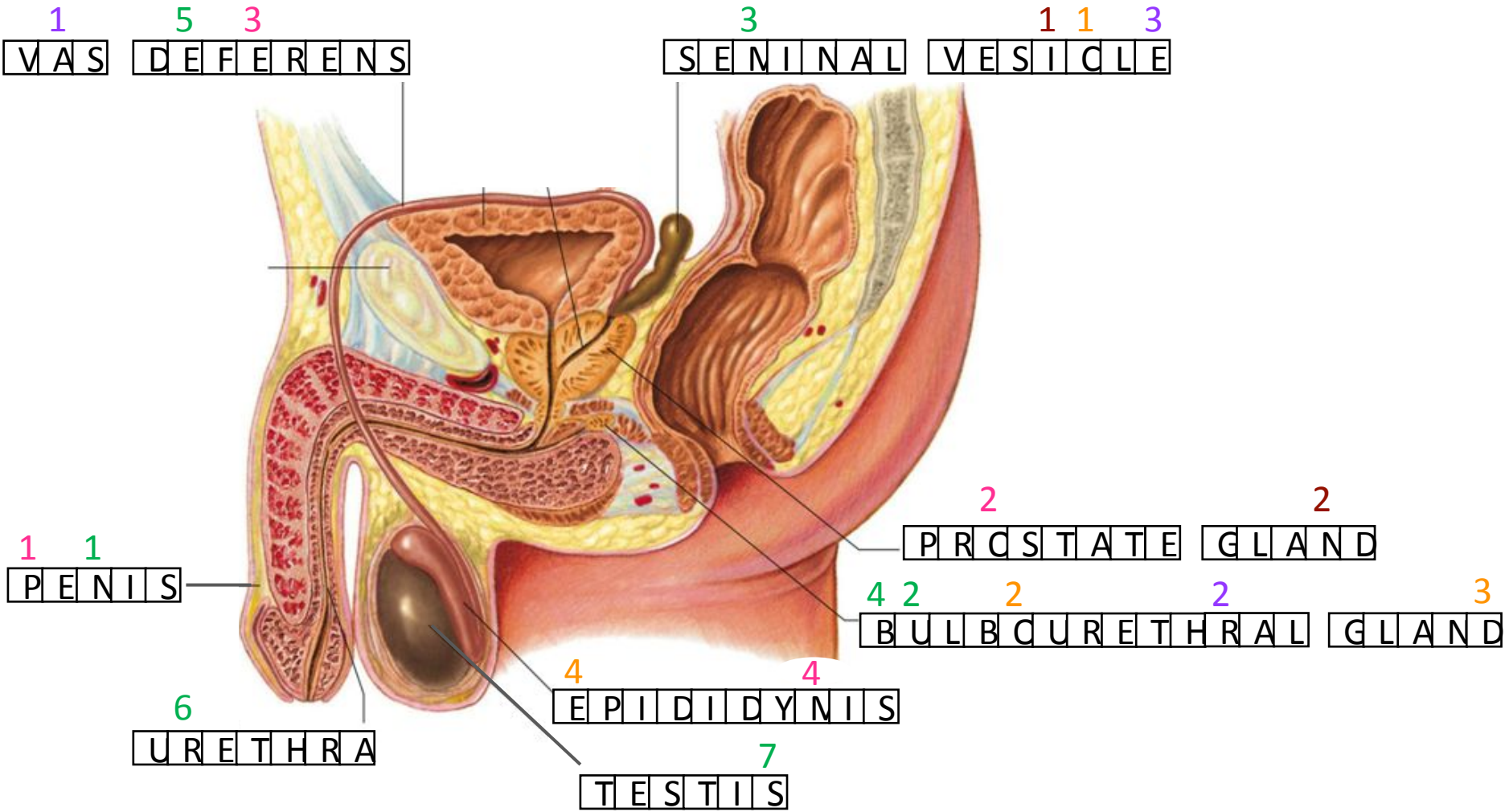
Guarding the testes further, two tunicas' vaginalis and albuginea  
Internal spermatic fascia should stop them getting broken  
Oh, why then does so much pain transmit these adventitia  
Spermatic cord encloses three arteries that supply the scrotum

Uniquely, the pampiniform venous veins cool the testes  
Mend the king's condition and you will be his bestie

--	--	--	--

Raise your hands when you have the code to unlock King  
Mikhail's second vlog entry

# ACTIVITY 2a -Answer



NUMBERS IN PCEM ARE CCDE

## ACTIVITY 2b -Answer

Scrotum is **one** sac of skin that hangs outside the body  
Parked within (this sac of skin) **two** organs known as testes  
Oh, why did evolution create a system quite so shoddy  
Now cremaster and dartos muscles must contract when it doth freeze



Guarding the testes further, **two** tunicas' vaginalis and albuginea  
Internal spermatic fascia should stop them getting broken  
Oh, why then does so much pain transmit these adventitia  
Spermatic cord encloses **three** arteries that supply the scrotum

Uniquely, the pampiniform venous veins cool the testes  
Mend the king's condition and you will be his bestie

1 2 2 3

Raise your hands when you have the code to unlock King  
Mikhail's first vlog entry

# ACTIVITY 1b -Answer



Corpus  
spongiosum

Scrotum is **one** sac of skin that hangs outside the body

Parked within (this sac of skin) **two** organs known as testes

Oh, why did evolution create a system quite so shoddy

Now cremaster and dartos muscles must contract when it doth freeze

Guarding the testes further, **two** tunicas' vaginalis and albuginea

Internal spermatic fascia should stop them getting broken

Oh, why then does so much pain transmit these adventitia

Spermatic cord encloses **three** arteries that supply the scrotum

Uniquely, the pampiniform venous veins cool the testes

Mend the king's condition and you will be his bestie

1 2 2 3

Raise your hands when you have the code to unlock King Mikhail's first vlog entry

# Vlog entry 2



# HEAD SCHOLARS – GATHER AT THE APOTHECARY

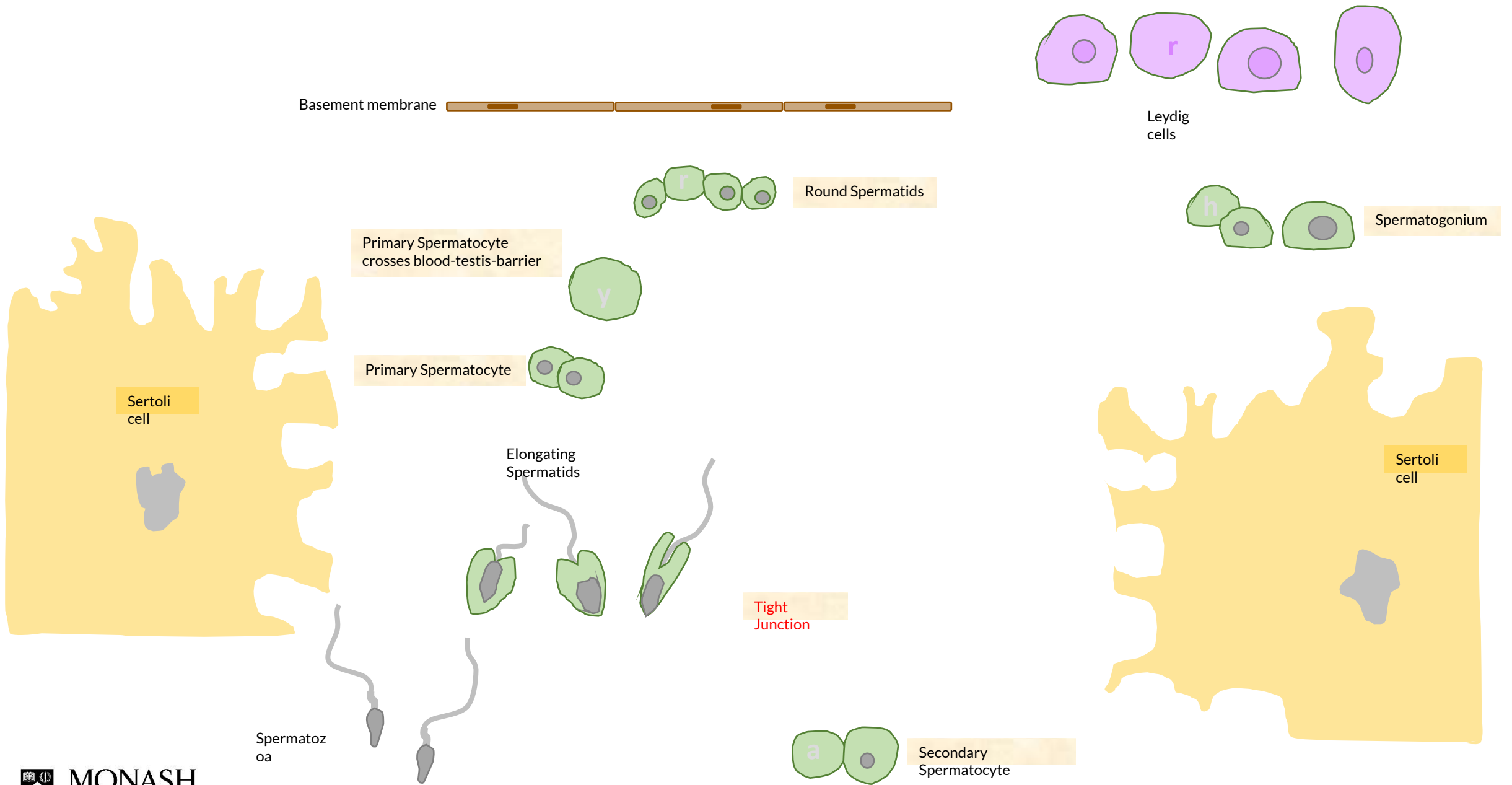


## ACTIVITY 3a

- Reconstruct the seminiferous epithelium and interstitial space.
- If reconstruction is correct, you will see some letters (from top to bottom)
- These letters will unlock the antique combination padlocks, which are in the Apothecary
- Open the lock to gain access to activity 3b

<https://www.timeanddate.com/stopwatch/>





# ACTIVITY 3b

Spermatogenesis

Hidden Word

Answer the **Clues** in the following order (might help you guess the code word):

11. The site of sperm production within the testis is the ..... tubule

4. Hypothalamic hormone that drives FSH and LH production is ..... releasing hormone

7. Sperm structure that contains hydrolytic enzymes that enable penetration of egg

2. Region of sperm that contains the genetic material

5. Hormone produced by Sertoli cells that negatively feeds back to the pituitary to suppress FSH synthesis

10. Name of testicular cells that respond to FSH and support spermatogenesis

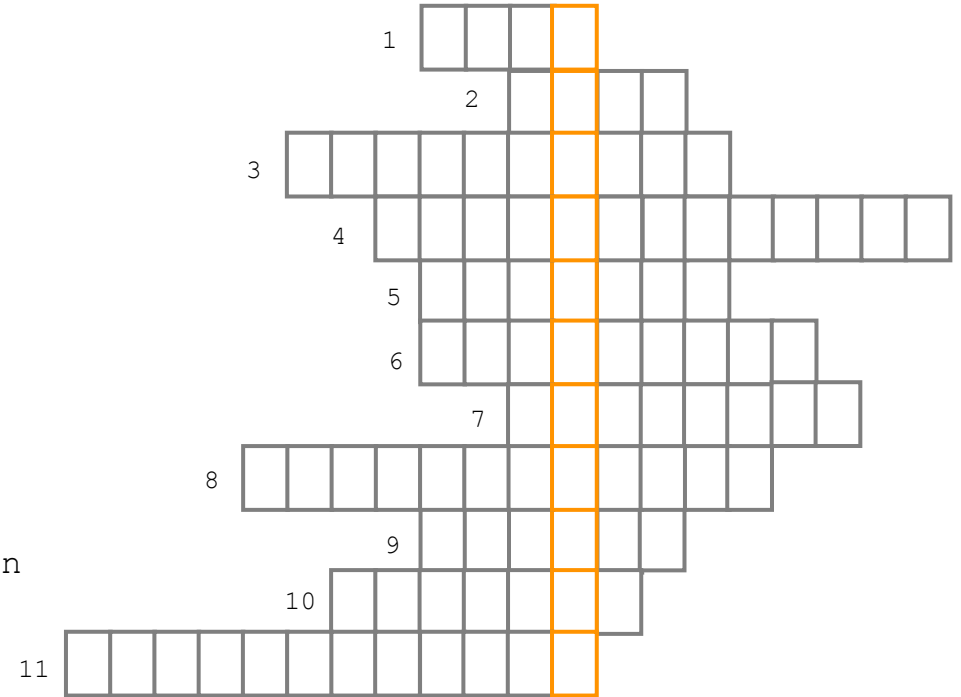
9. Number of stages in the spermatogenic cycle in humans

3. Stores and protects spermatozoa, while facilitating functional maturation

1. The region of sperm that propels it through the female reproductive tract

6. The mid-piece of sperm contains mitochondria that provide energy for the whip-like movements of the .....

8. A hormone produced by Leydig cells

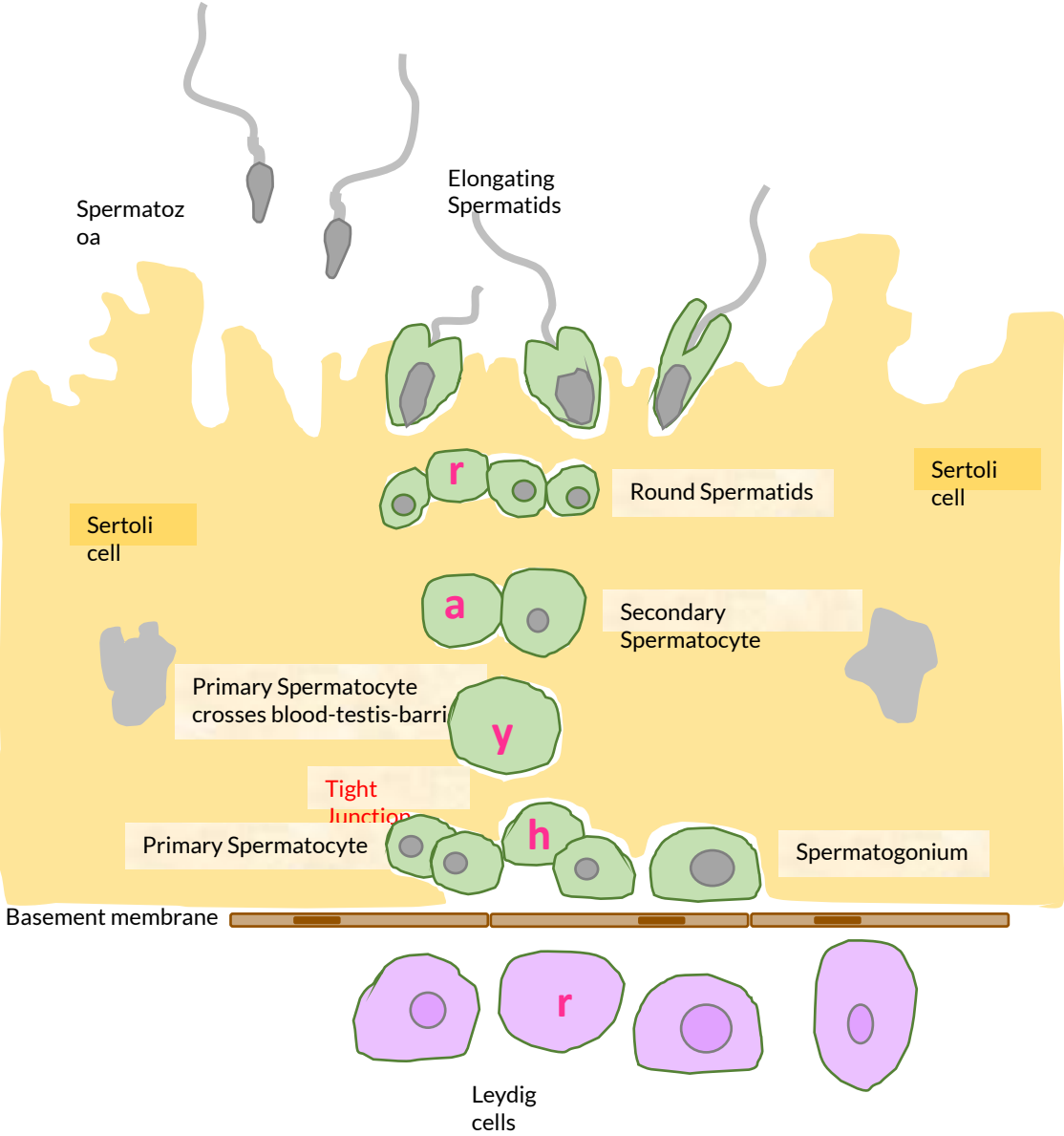


Transpose the code to unlock Ari's second vlog



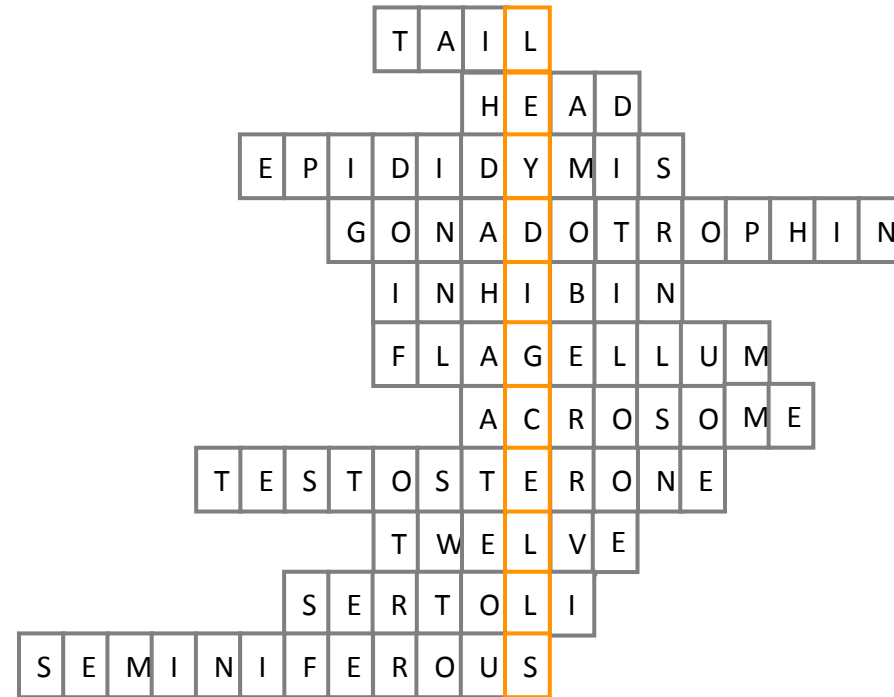
Raise your hands when you have the answer

# ACTIVITY 3a -Answer



# ACTIVITY 3b

-Answer



Transpose the code to unlock Video

3

L E Y D I G C E L L S

# Vlog entry 3



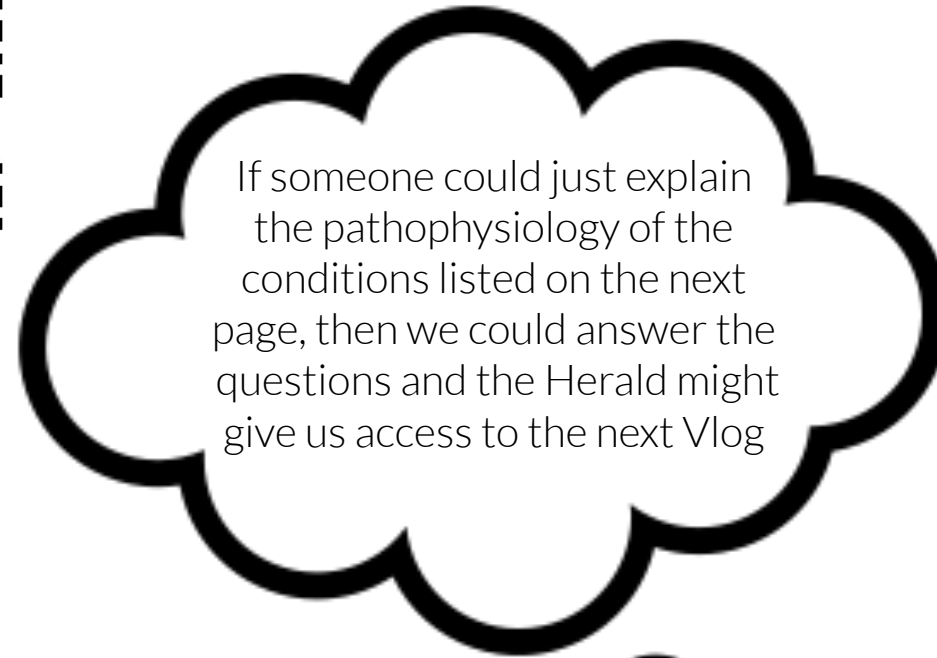
# HEAD SCHOLARS – GATHER AT THE APOTHECARY





<https://www.timeanddate.com/stopwatch/>

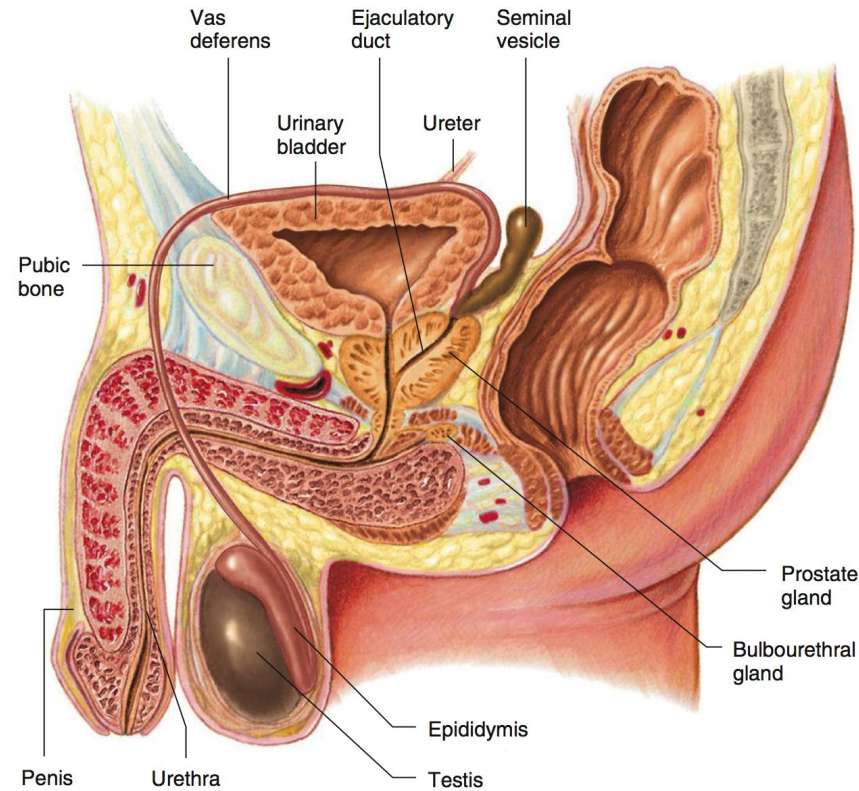
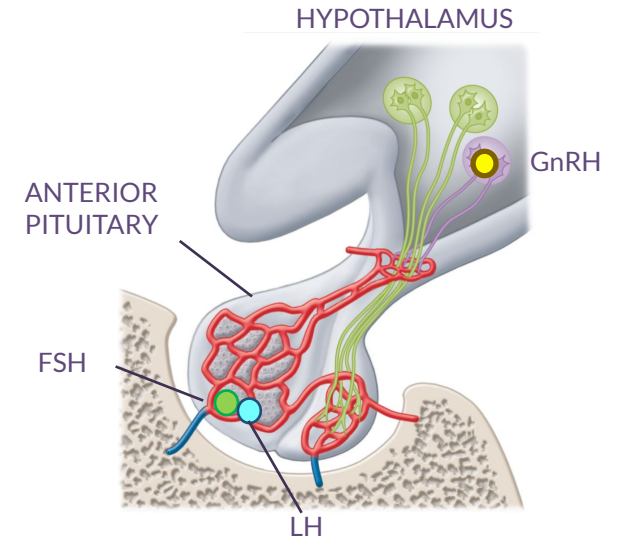
# ACTIVITY 4



# ACTIVITY 4B

Identify:

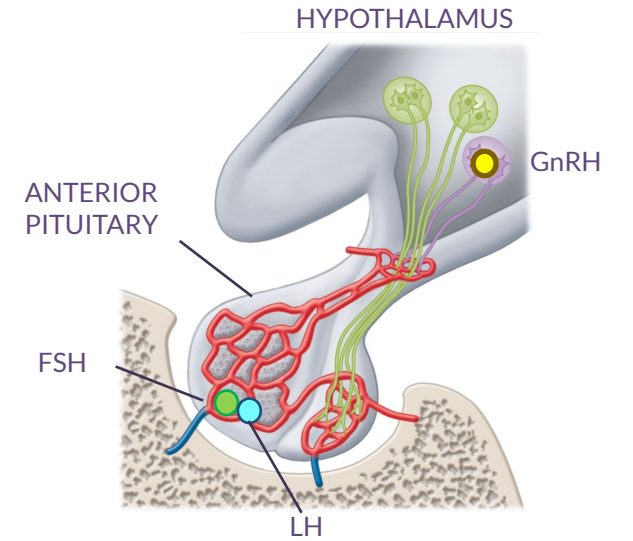
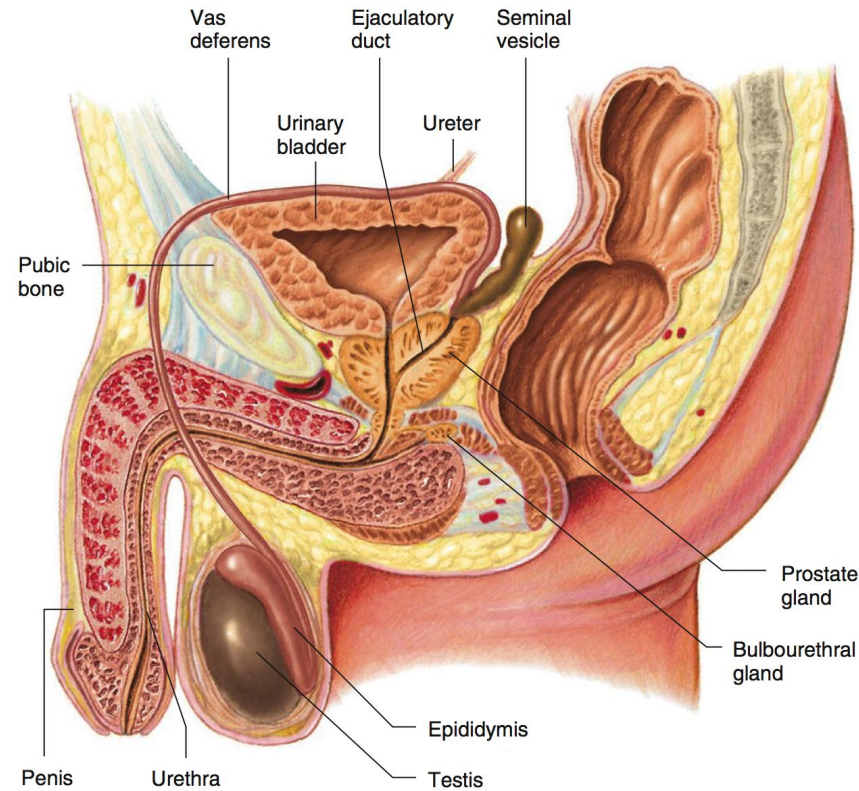
1. Three sites that could be affected in Obstructive Azoospermia
2. The site affected by Primary Hypogonadism
3. The sites affected by Hypogonadotropic Hypogonadism
4. The site affected by SV agenesis
5. The site targeted in a Vasectomy



# ACTIVITY 4

Identify:

1. Three sites that could be affected in Obstructive Azoospermia  
**Epididymis, Vas deferens, Ejaculatory duct**
2. The site affected by Primary Hypogonadism  
**Testes**
3. The sites affected by Hypogonadotropic Hypogonadism  
**Hypothalamus, Pituitary**
4. The site affected by SV agenesis  
**Seminal vesicle**
5. The site targeted in a Vasectomy  
**Vas deferens**



# ACTIVITY 4

THE CODE WORD IS THERE, SOMEWHERE .....



# ACTIVITY 4

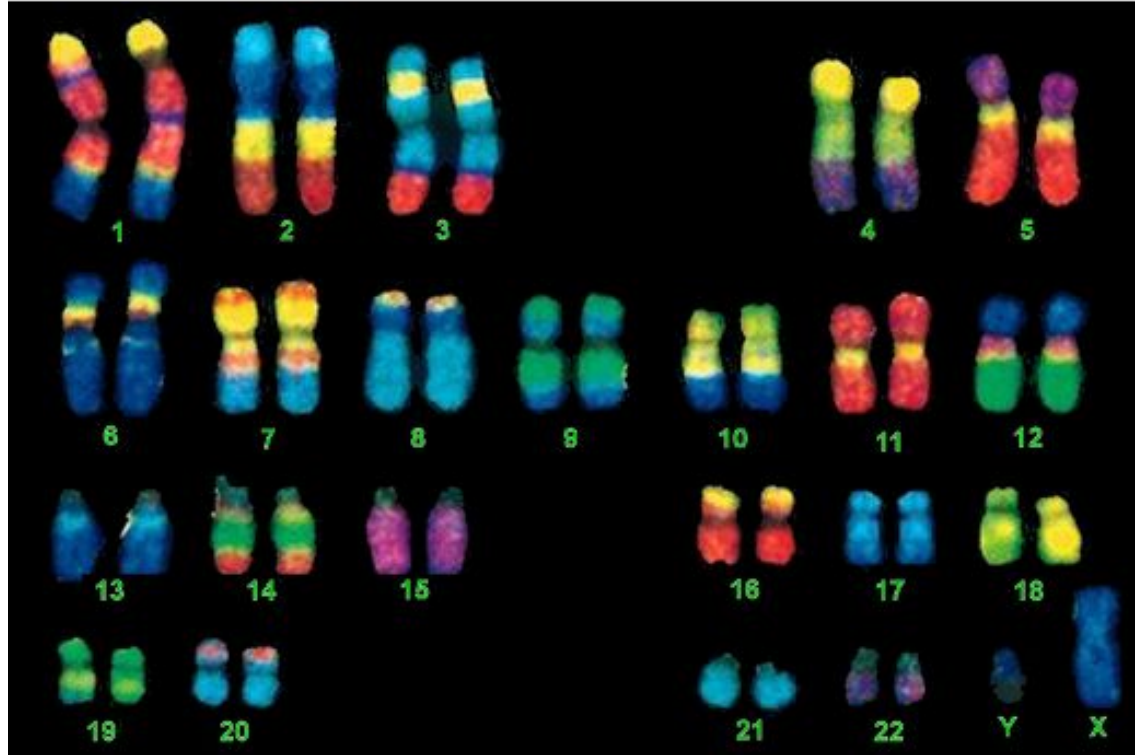
THIS MIGHT HELP?



# Vlog entry 4



Mikhail seemed proud of his karyotype – maybe it's important?



Hand out with Activity 5

# HEAD SCHOLARS – GATHER AT THE APOTHECARY





<https://www.timeanddate.com/stopwatch/>

# ACTIVITY 5

## Case Study – Infertility in pesticide (DBCP) workers

(From: The National  
Academies of Sciences,  
Engineering and Medicine)

COMPARISON OF NON-VASECTOMISED DBCP WORKERS WITH VERY LOW (GROUP A) AND  
NORMAL (GROUP B) SPERM COUNTS

Group	Number of Subjects	Age (years)	Exposure (years)	Sperm count ( $10^6$ /ml)	FSH (mIU/ml)	LH (mIU/ml)	Testosterone (ng/dl)	Inhibin (pg/ml)
A	11	33*	8*	0.2**	9**	15	468	37**
B	11	27*	0.1*	93**	2.5**	14	459	216**

\*Difference between groups A and B significant at  $P < 0.01$

\*\*Difference between groups A and B significant at  $P < 0.001$

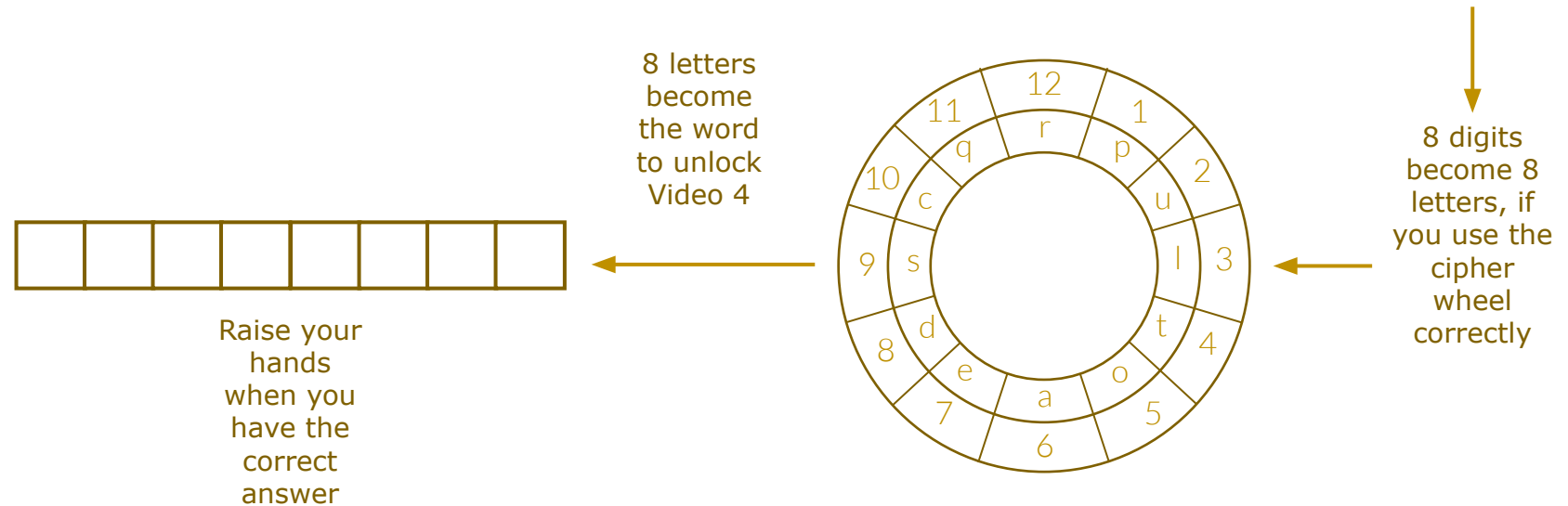
# ACTIVITY 5

## Case Study – Infertility in pesticide (DBCP) workers

(From: The National  
Academies of Sciences,  
Engineering and Medicine)

QUESTIONS RELATE TO DATA IN PREVIOUS TABLE

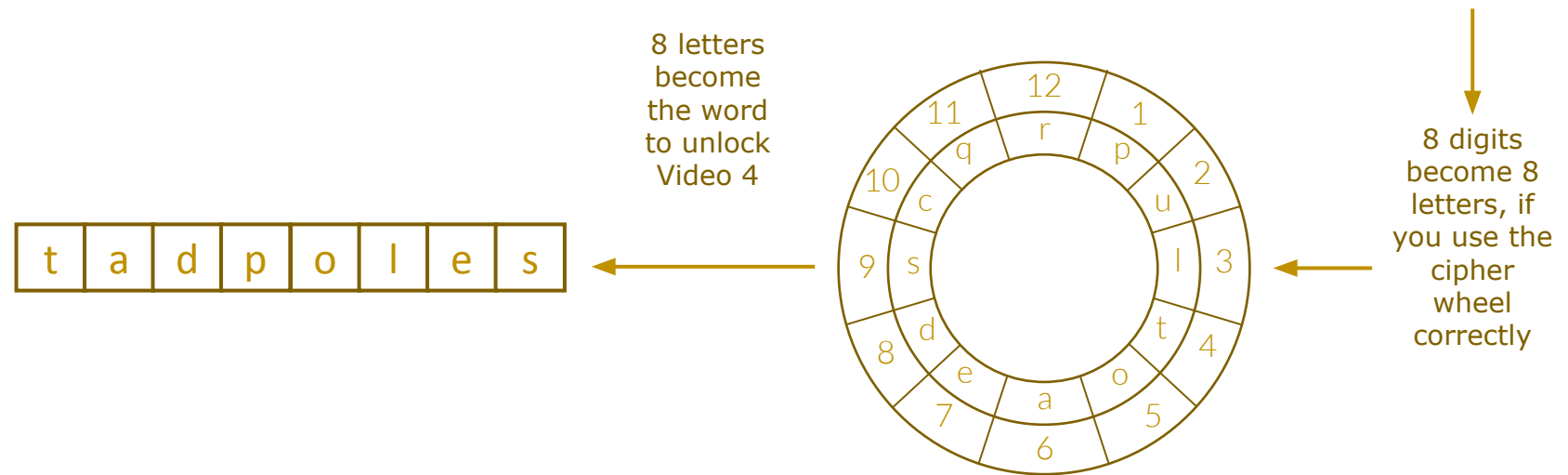
	Hormone	Value in affected men (number only)
1. The levels of which hormone in affected men suggests DBCP does not damage Leydig cells?		
2. Normal levels of the above Leydig cell hormone ensure negative feedback to which pituitary hormone?		
3. The levels of which hormone in affected men suggests DBCP damages Sertoli cells?		
4. A loss of negative feedback from Sertoli cells affects which hormone's production?		



# ACTIVITY 5 - Answer

QUESTIONS RELATE TO DATA IN PREVIOUS TABLE

	Hormone	Value in affected men (number only)
1. The levels of which hormone in affected men suggests DBCP does not damage Leydig cells?	Testosterone	468
2. Normal levels of the above Leydig cell hormone ensure negative feedback to which pituitary hormone?	LH	15
3. The levels of which hormone in affected men suggests DBCP damages Sertoli cells?	Inhibin	37
4. A loss of negative feedback from Sertoli cells affects which hormone's production?	FSH	9



# Vlog entry 5



# HEAD SCHOLARS – GATHER AT THE APOTHECARY





<https://www.timeanddate.com/stopwatch/>

PICTURE  
START

# ACTIVITY 6

A male contraceptive pill?

1. Watch the Video
2. Read through the 5 facts and jot down on your tables how WIN-18446 blocks spermatogenesis
3. Once you have the mechanism sorted, call a herald who will provide you with the activity to gain access to King Mikhail's final Vlog entry
4. Once you have the code word, call the Herald back



# ACTIVITY 6

## Fact #1 (Excerpt from Bloomberg Businessweek (3-8-17) by Emily Anthes)

The trouble began, as it so often does, with a bottle of Chivas Regal. Back in the 1950s, scientists at Sterling Drug, a now-defunct pharmaceutical company, synthesized a class of chemicals that made male rats temporarily infertile. They thought they might be onto something big: the first-ever birth control pill—for men. After identifying several promising compounds, including one known as WIN 18,446, a trio of researchers began testing them on a ready population, inmates at the Oregon State Penitentiary.

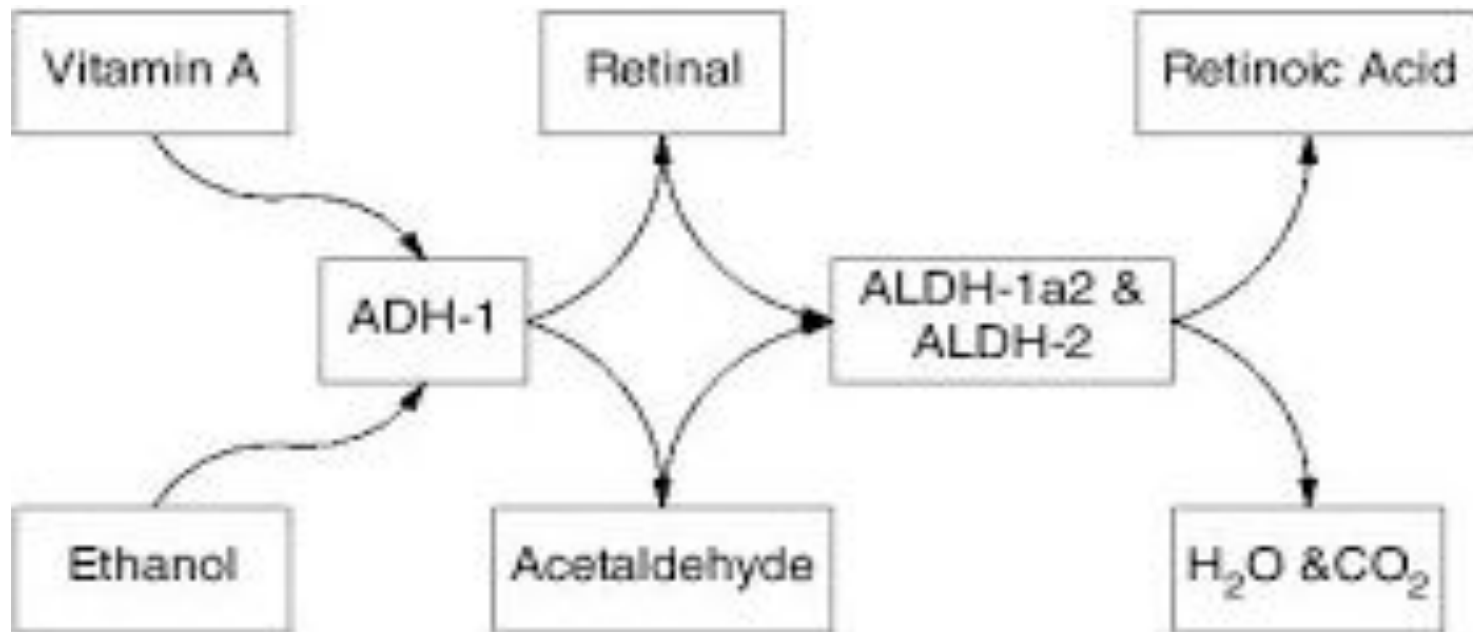
The results were astonishing. Within 12 weeks, the inmates' sperm counts had plummeted. When the men stopped taking the drugs, sperm production returned to normal. Better yet, they experienced few side effects.

Then one of the participants drank some contraband Scotch and became unusually, violently ill. He confessed his transgression to the researchers, and follow-up studies confirmed his account: WIN 18,446 didn't mix well with booze. Men who combined the two reported heart palpitations, sweating, nausea, and vomiting.

The research was quietly abandoned ...

# ACTIVITY 6

Fact #2 (Proceedings of the Australian Physiological Society 43:17-24)



# ACTIVITY 6

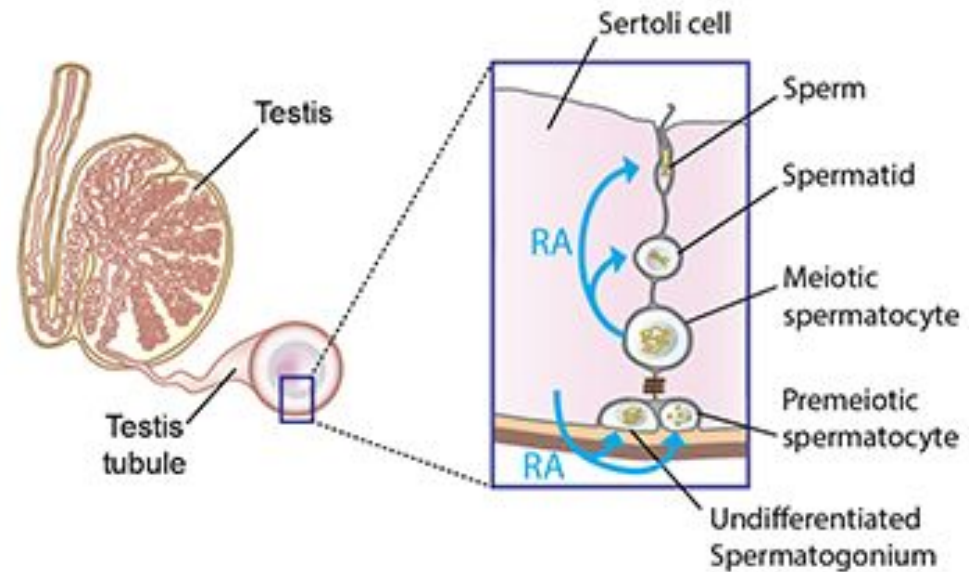
## Fact #3 (Excerpt from Bloomberg Businessweek (3-8-17) by Emily Anthes)

Antabuse (disulfiram) is prescribed to patients who struggle with alcohol addiction. The drug blocks most forms of the enzyme acetaldehyde dehydrogenase (ALDH), which helps the body metabolize alcohol; drinking while taking disulfiram leads to an extremely unpleasant, and occasionally fatal, constellation of hangover-like symptoms.

# ACTIVITY 6

## Fact #4 (Endo et al PNAS 2017 doi:10.1073/pnas.1710837114)

“Authors show that retinoic acid (RA), a derivative of vitamin A, is required for differentiation and meiosis during spermatogenesis.



# ACTIVITY 6

## Fact #5 (Excerpt from Bloomberg Businessweek (3-8-17) by Emily Anthes)

There are almost 20 different forms of ALDH; the liver relies primarily on ALDH2 to metabolize alcohol, while the testes use ALDH1A2 to make retinoic acid.

## ACTIVITY 6

WIN-18,446 failed as a male contraceptive because it \_\_\_\_\_ multiple forms of the enzyme acetaldehyde dehydrogenase

<https://mywordle.strivemath.com/?word=ohziwio>

# Vlog entry 6



# HEAD SCHOLARS – GATHER AT THE APOTHECARY





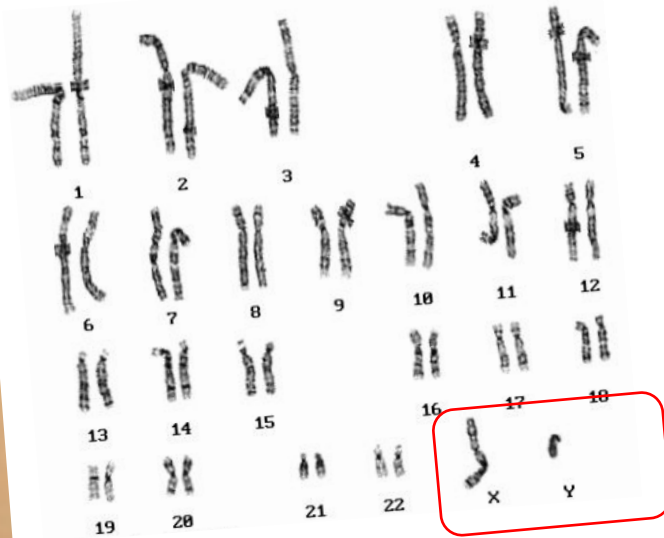
<https://www.timeanddate.com/stopwatch/>

# Potential causes of Mikhail's infertility

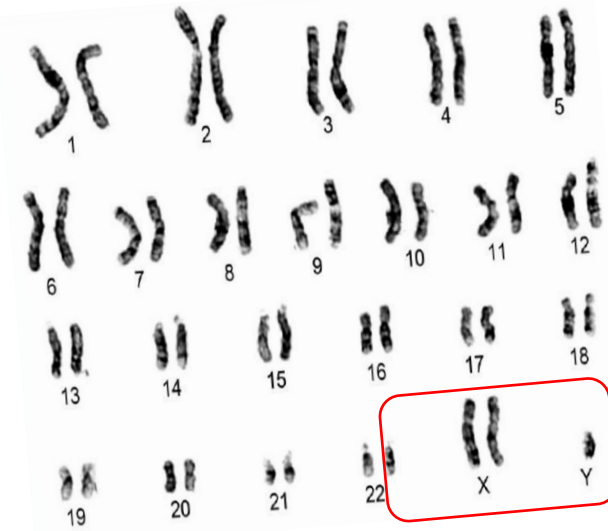


# Potential causes of Mikhail's infertility

**Klinefelter syndrome** has an estimated frequency of 1 in 600 in the general population. Affected individuals typically have small, firm testes with hyalinization of seminiferous tubules and consequent spermatogenic failure (>90% of men have azoospermia and the remaining men have severe oligospermia)



Normal Male  
Karyotype



Klinefelter's  
Karyotype

# Potential causes of Mikhail's infertility



## Anabolic steroids making musclemen infertile, say doctors

Bodybuilders destroying their chance of becoming fathers in their quest to bulk up, specialists report



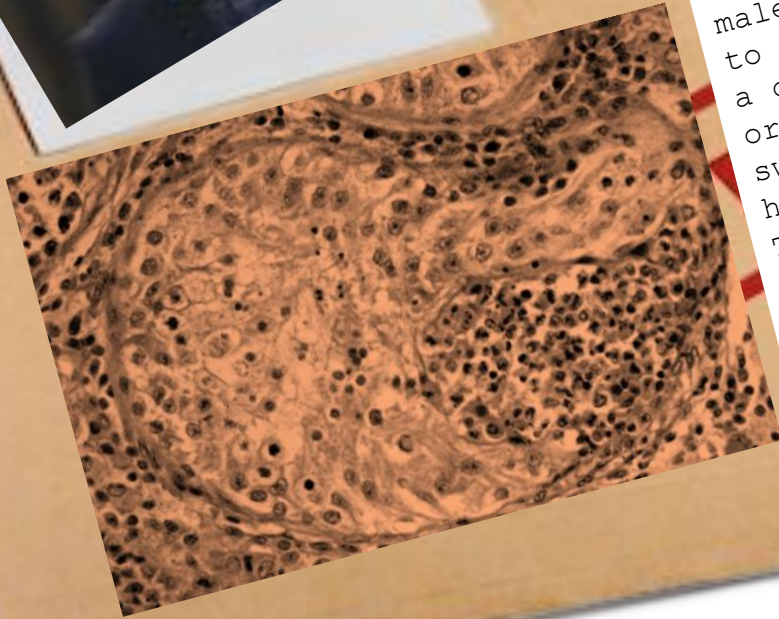
▲ "These patients walk through the door looking like Arnold Schwarzenegger in his younger days," said Dr Allan Pacey. Schwarzenegger - pictured in 1977 - has said he took steroids when they were legal. Photograph: Everett Collection/Rex Features

Growing numbers of men are becoming infertile because they take anabolic steroids in their quest for a muscular body, doctors have warned.

Urologists are seeing more and more men whose difficulty in becoming a father is linked to consumption of the muscle-boosting drugs.

Steve Payne, a consultant urologist at the Manchester Royal Infirmary and a council member of the British Association of Urological Surgeons, said: "Many fit young men who believe they are at the peak of physical perfection don't believe it could be their fault when their wives or girlfriends find it difficult to become pregnant."

# Potential causes of Mikhail's infertility



## **Mumps Orchitis**

Mumps is a viral disease classically associated with painful swelling of the salivary glands next to the ears. In 20-30% of mumps cases in post-pubescent males, the disease spreads to the testes, resulting in a condition called mumps orchitis. Symptoms include swelling, inflammation and hemorrhaging in the testes. The combination of hostile environment and raised pressure can lead to residual atrophy and subfertility. The MMR vaccine is a vaccine against measles, mumps, and rubella.

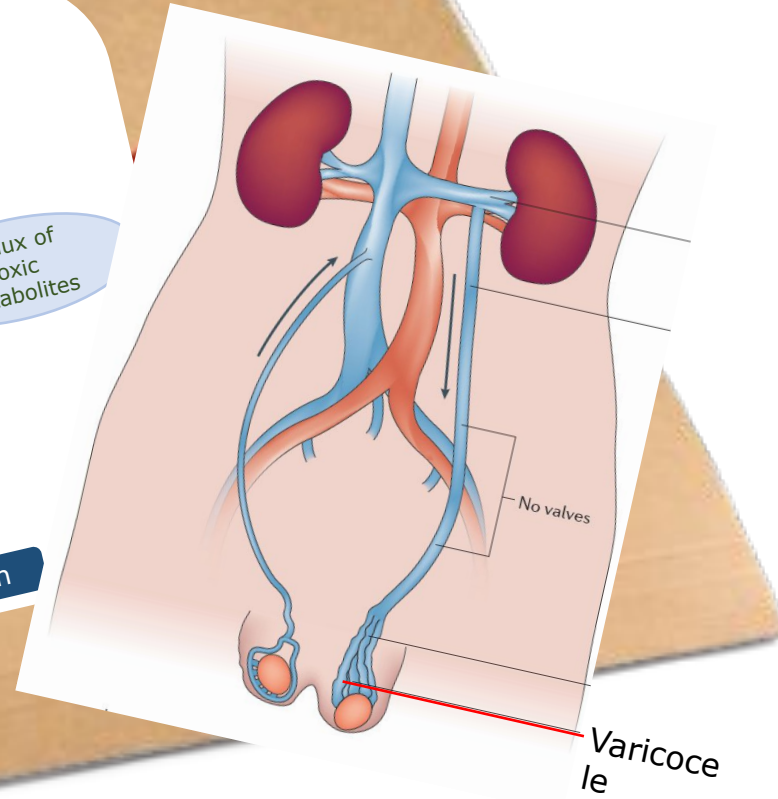
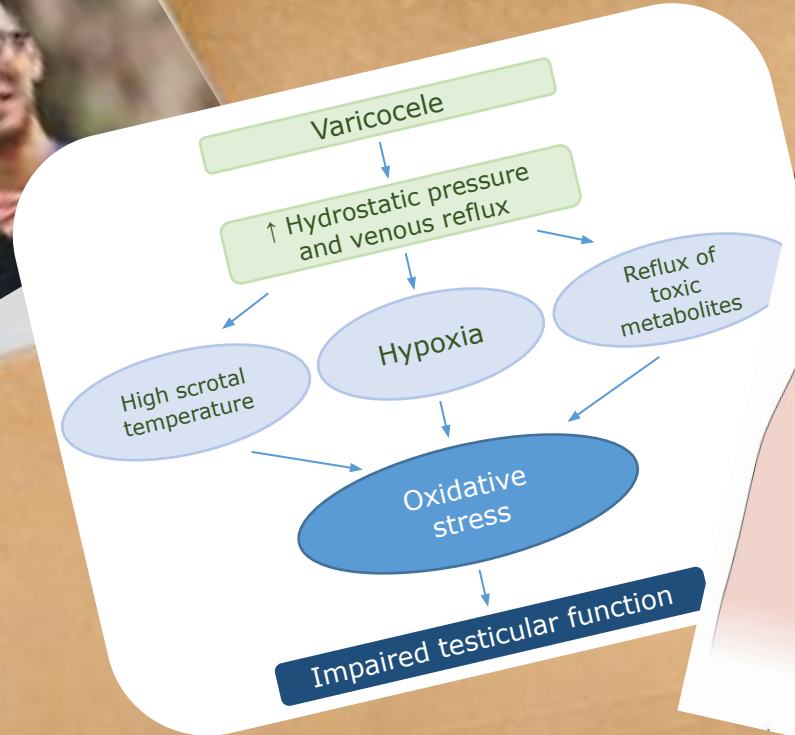
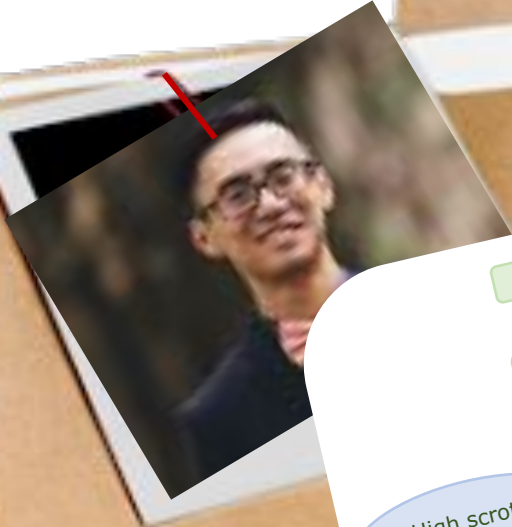
# Potential causes of Mikhail's infertility



# Potential causes of Mikhail's infertility



# Potential causes of Mikhail's infertility



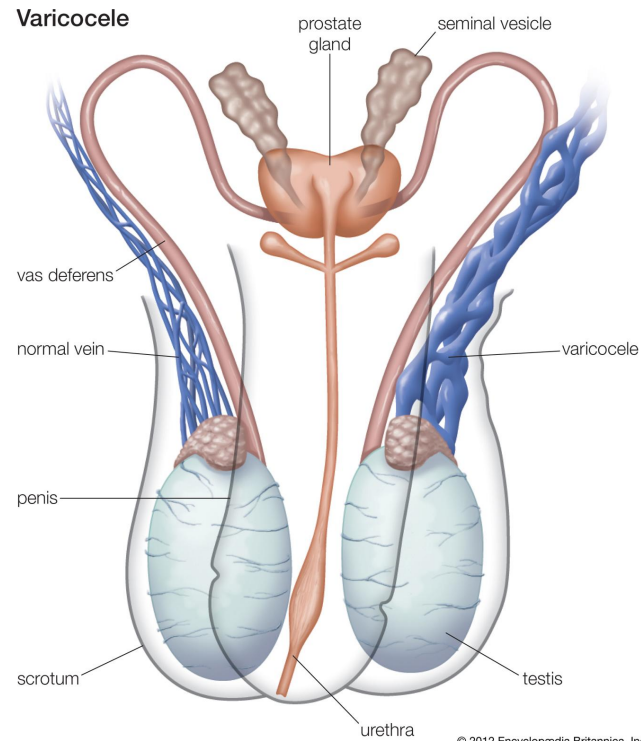
# FINAL DIAGNOSIS AND TREATMENT

- SIX choices: (1) Klinefelter's syndrome (2 right – 8 left)
- (2) Anabolic steroid use (4 right – 1 left)
  - (3) Mumps Orchitis (8 right – 8 left)
  - (4) Vasectomy (6 right – 3 left)
  - (5) Abnormal morphology and motility (2 right – 5 left)
  - (6) Varicocele (3 right – 6 left)

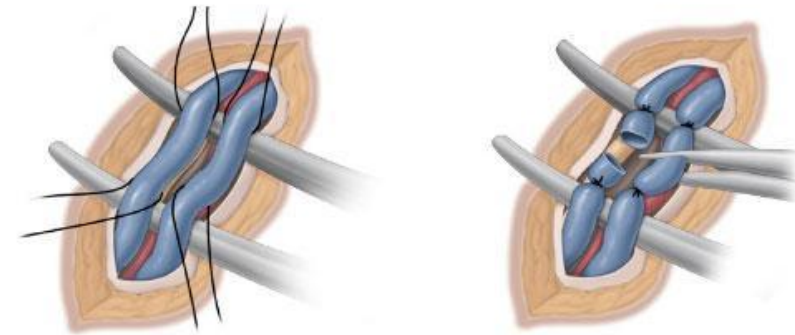
Your answer (if correct) will open the strongbox in the Apothecary

# FINAL DIAGNOSIS AND TREATMENT

- (6) **Varicocele:** An enlargement of a vein within the scrotum. A varicocele can cause poor development of the testes, low sperm count and infertility in some cases.



© 2012 Encyclopædia Britannica, Inc.



Varicolectomy can remove enlarged veins (via ligation) and improve fertility

You chose ...



You chose ...



# Mikhail's complete medical history

	<b>King Mikhail says:</b>
<b>Video 1</b>	I've never had elective surgery in my life
<b>Video 2</b>	My sperm look great and move really well
<b>Video 3</b>	I have trypanophobia, which is an extreme fear of needles
<b>Video 4</b>	I had my chromosomes karyotyped
<b>Video 5</b>	My scrotal temperature is tremendously high
<b>Video 6</b>	My mother made me have the MMR vaccine when I was young

“HALT!”

