

# BIOCHEMISTRY

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USMLE step 1

# Question 1

- A 6-year-old presents to his pediatrician with skin lesions all over his body. For several years he has been very sensitive to sunlight. Neither the boy's parents nor his siblings have the same skin lesions or sun sensitivity. Biopsies of several of the boy's lesions reveal squamous cell carcinoma. Which mutation would one expect to see in this patient's DNA?
- A, Methylation of the gene
- B, Missense mutation in the gene
- C, Nonsense mutation in the middle of the gene
- D, Point mutation within the enhancer region
- E, Point mutation within the operator region
- F, Point mutation within the promoter region
- G, Thymidine dimers

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# Question 1

- Patients with inherited disorder, ... , are at increased risk for the development of cancers (**basal cell carcinoma, squamous cell carcinoma, malignant melanoma**) of sun-exposed skin. The basis for this disorder is defective DNA repair. UV rays in sunlight cause **cross-linking of pyrimidine residues**, preventing normal DNA replication. Such DNA damage is repaired by the nucleotide excision repair system. Several proteins are involved in nucleotide excision repair, and an inherited loss of any of these can give rise to ... .

# Question 1

- Patients with inherited disorder, **xeroderma pigmentosum**, are at increased risk for the development of cancers (**basal cell carcinoma, squamous cell carcinoma, malignant melanoma**) of sun-exposed skin. The basis for this disorder is defective DNA repair. UV rays in sunlight cause **cross-linking of pyrimidine residues**, preventing normal DNA replication. Such DNA damage is repaired by the nucleotide excision repair system. Several proteins are involved in nucleotide excision repair, and an inherited loss of any of these can give rise to **xeroderma pigmentosum**.

# Nucleobases

## PURines

- Adenine
- Guanine
- **PUR**e **A**s **G**old

## PYrimidines

- Cytosine
- Uracil
- Thymine
- **CUT** the **PY** (pie)

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# Question 1 - Thinking outside the box

- Autosomal recessive/dominant
- X-linked recessive/dominant
  
- What is the zygosity of the boy's parents with respect to the gene in question?

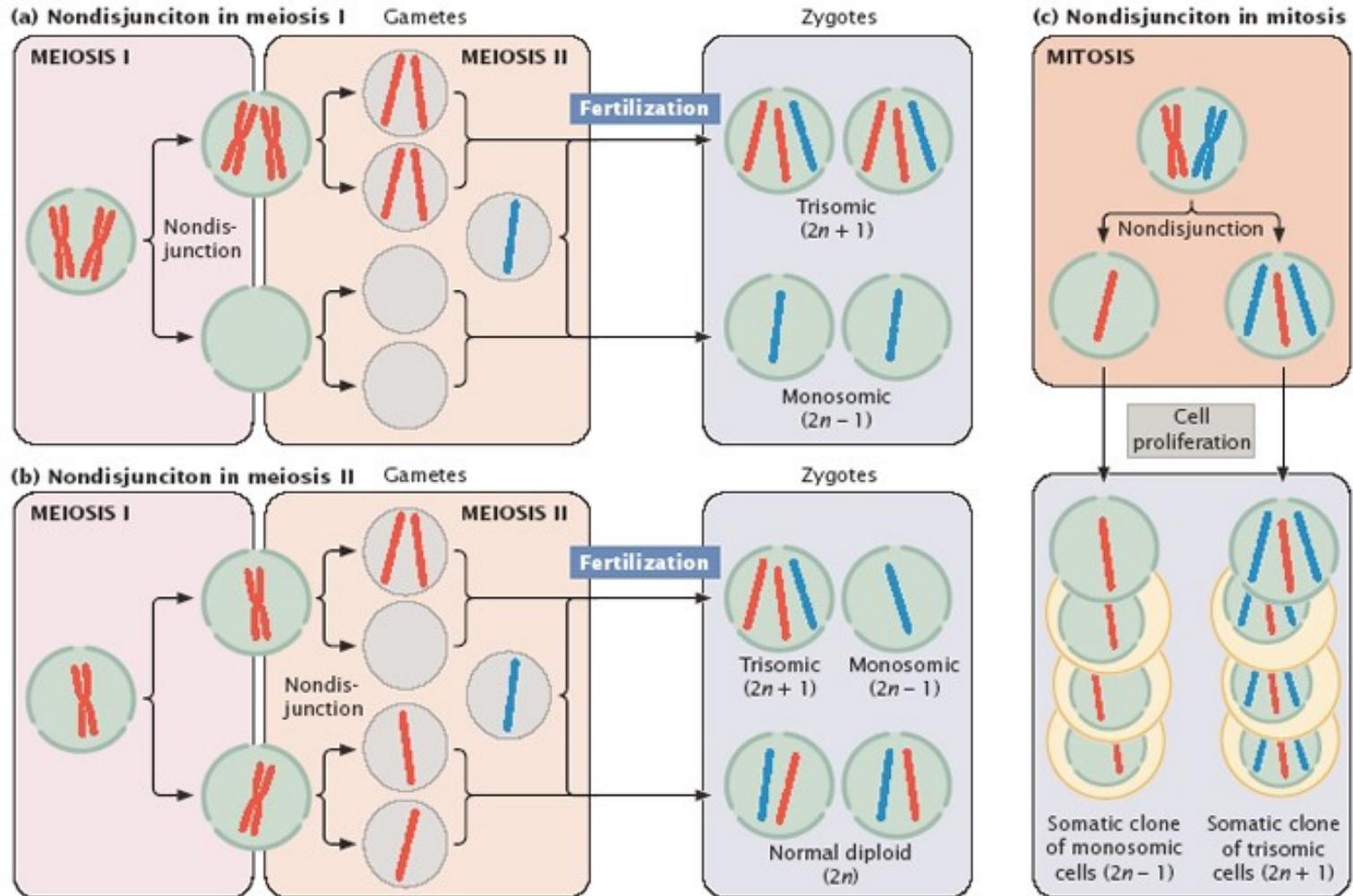
# Question 1 - Thinking outside the box

- What if DNA analysis shows that only one of the parents is a carrier?
  - Sequencing error
  - One of the parents is not an actual biological parent
  - Something else

# Question 1 - Thinking outside the box

- Something else
  - Uniparental disomy
    - Offspring receives 2 copies of a chromosome from 1 parent and no copies from the other parent
    - Heterodisomy
      - Nondisjunction at meiosis 1
    - **Isodisomy**
      - Nondisjunction at **meiosis 2**
      - Postzygotic chromosomal duplication of one of a pair of chromosomes, and loss of the other of the original pair

# Nondisjunction



## Question 2

- A 32-year-old develops polyuria. Her nephrologist monitors her closely on a water deprivation test, and she continues to have increased urine output. A diagnosis of diabetes insipidus is made. The nephrologist orders an antidiuretic hormone level and determines that it is slightly increased. Which of the following is the site of pathology in this patient?
- A, Adenohypophysis
- B,  $D_1$
- C, Pituitary function
- D,  $V_1$
- E,  $V_2$

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# Diabetes insipidus

- ADH (vasopressin) issue
- Clinical findings
  - Intense thirst
  - Polyuria
- Lab
  - Urine specific gravity  $<1.006$
  - Serum osmolarity  $>290$  mOsm/L

# Diabetes insipidus

## Central

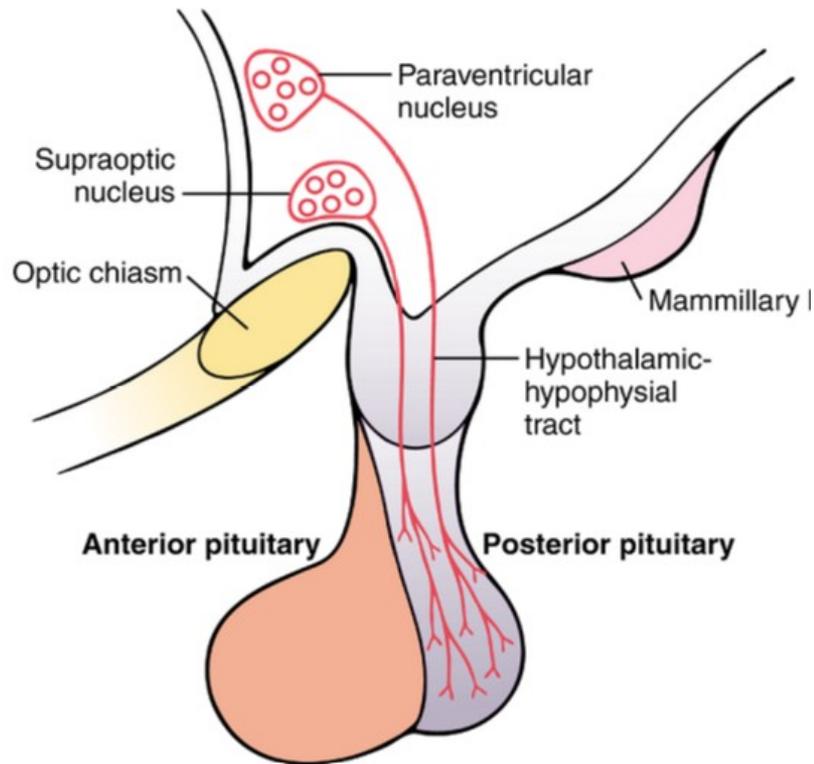
- ADH deficiency
- Causes
  - Head trauma
  - Neoplasms
  - Inflammatory disorders
  - Surgical procedures

## Nephrogenic

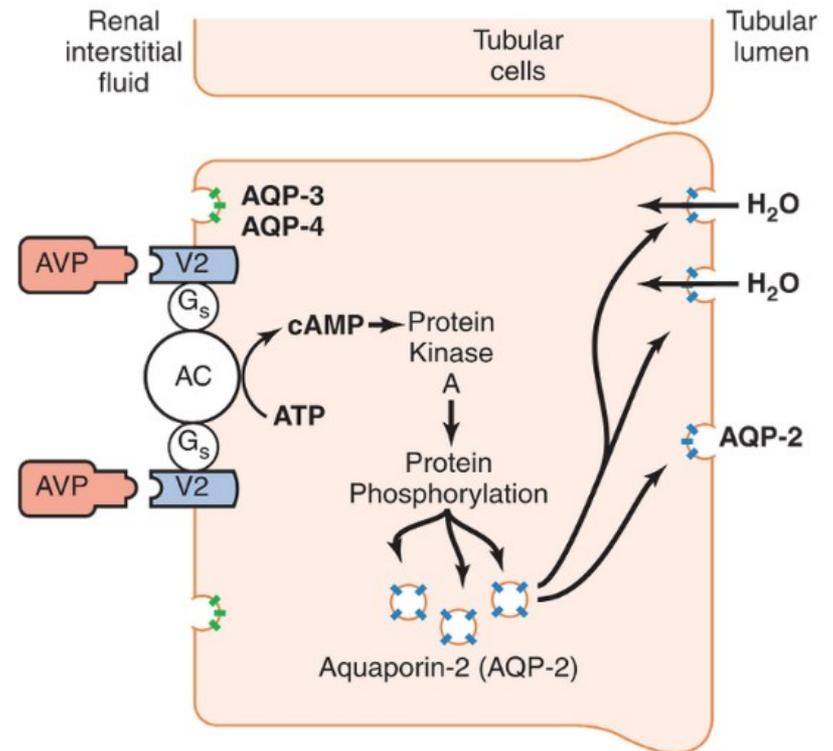
- Renal tubular unresponsiveness
- Vasopressin receptors
  - $V_1$  on vascular smooth muscles → vasoconstriction
  - $V_2$  on late distal tubules, collecting tubules and collecting ducts → water reabsorption
  - $V_3$  in pituitary

# Diabetes insipidus

## Central



## Nephrogenic



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# Bibliography

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- *Rapid Review Pathology*, Goljan et al.
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