Diabetes Insipidus

Presented By :
Qahtan Saraireh
Aseel Qudah
Mu’mn Saraireh
Supervised by: Dr.Ahmad Tarawneh

Mutah University | 2025

Overview

- DEFINITION OF DI
- ADH PHYSIOLOGY
- ADH FUNCTION ON THE NEPHRONS
- TYPES OF DI
- CLINICAL FEATURES
- DM VS DI
- DIAGNOSES
- WATER DEPRIVATION TEST
- MANAGEMENT
- TREATMENT
- REFERENCES

Definition of DI

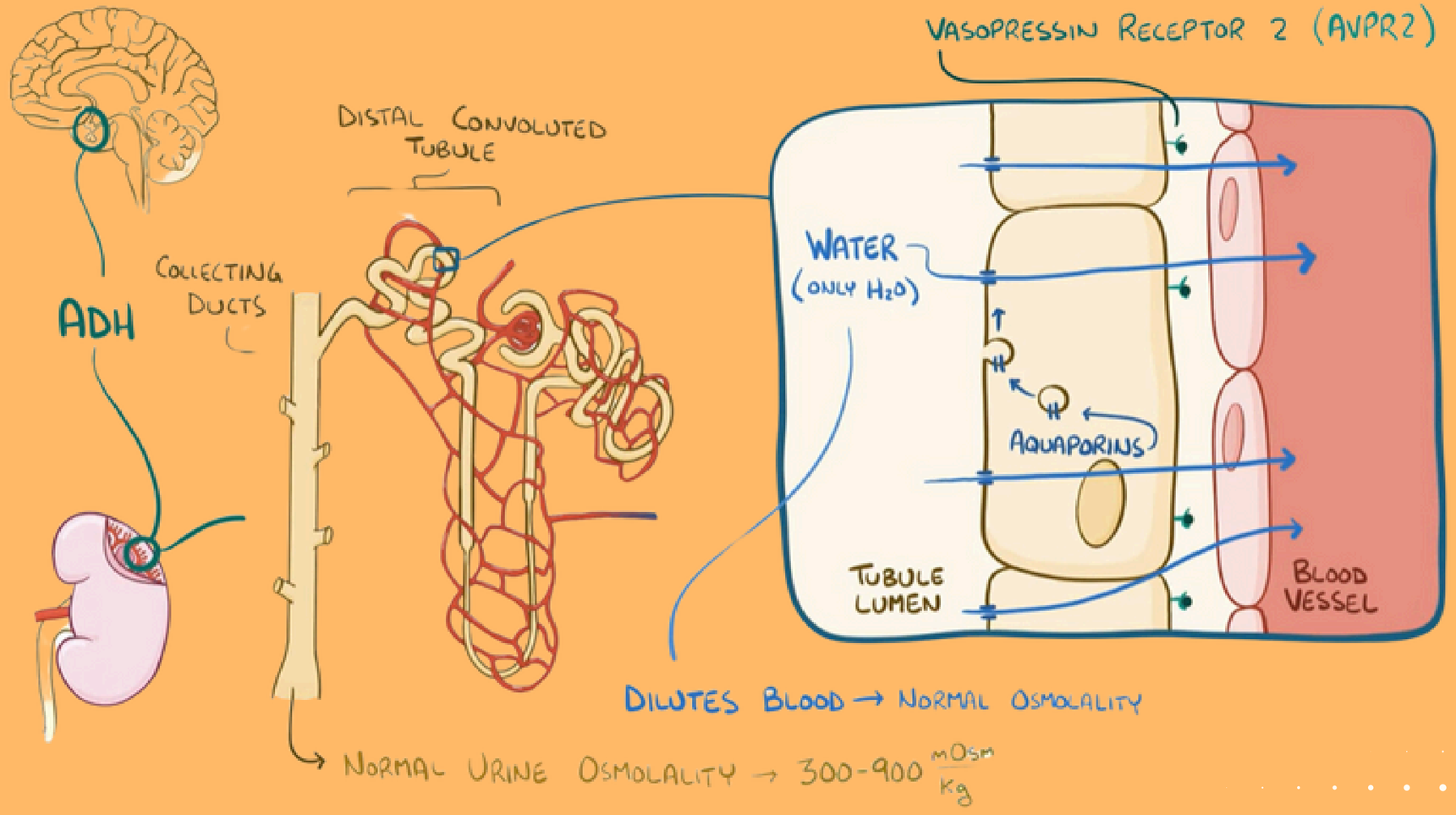
Diabetes insipidus occurs when the kidneys are unable to retain free water, causing a dilute urine despite progressively increasing plasma osmolality . It’s characterized by thirst (polydipsia) & polyuria (5-20L/day).

OSMOLALITY : IS THE CONCENTRATION OF DISSOLVED PARTICLES IN THE BLOOD PLASMA

*GLUCOSE *NA *BLOOD UREA NITROGEN

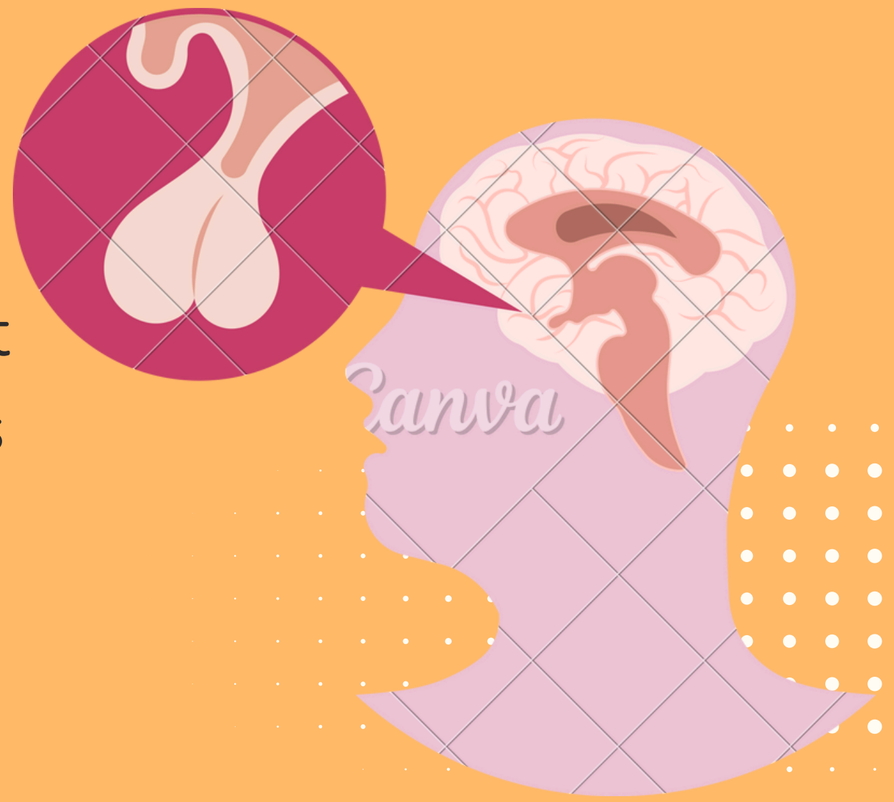
ADH physiology

ADH physiology



ADH Physiology

Vasopressin or antidiuretic hormone (ADH) or arginine vasopressin (AVP) is synthesized in the hypothalamus and stored in the posterior pituitary (neurohypophysis). Science has known it to play essential roles in the control of the body's osmotic balance, blood pressure regulation, sodium homeostasis, and kidney functioning.

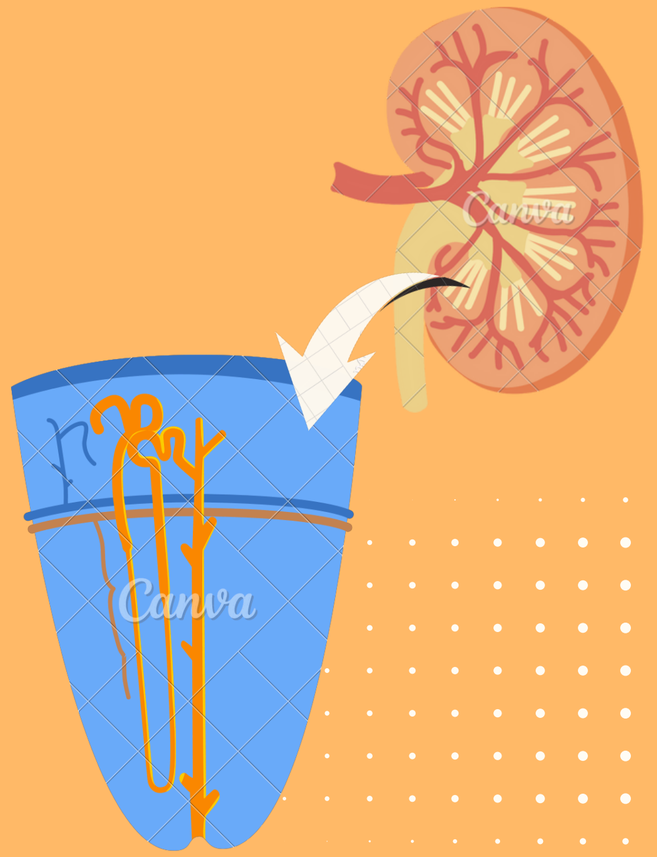


ADH Physiology

ADH is stored in neurons within the hypothalamus. These neurons express osmoreceptors that are exquisitely responsive to blood osmolarity and respond to changes as little as [2] mOsm/L. Therefore, slight elevations in osmolarity result in the secretion of ADH. ADH then acts primarily in the kidneys to increase water reabsorption, thus returning the osmolarity to baseline.

ADH function on the nephrons

ADH primarily affects the ability of the kidney to reabsorb water in the late distal tubule and collecting duct. In states of hypovolemia or hypernatremia, ADH is released from the posterior pituitary gland and binds to the type-2 receptor (V2) in principal cells of the collecting duct which facilitates Aquaporin (AQP)-mediated water reabsorption, then after achieving water homeostasis, the ADH level decreases .



TYPES OF DI

Types Of DI

Central Diabetes Insipidus
(Arginine Vasopressin Deficiency)

Nephrogenic Diabetes Insipidus
(Arginine Vasopressin Resistance)

GESTATIONAL DIABETES INSIPIDUS

DIPSOGENIC DIABETES INSIPIDUS

CENTRAL DIABETES INSIPIDUS

(Arginine vasopressin deficiency)

1. AVP-D is caused by the inability of the neurohypophysis to synthesize and/or secrete AVP in response to increased plasma osmolality. Damage or dysfunction of any part of the neurohypophysis, if sufficiently severe, can cause AVP-D. Normal function of only 10 to 15 percent of the AVP-producing neurons is generally sufficient to secrete enough AVP to prevent symptoms.

2. AVP-D may also result from dysfunction of osmoreceptors in the hypothalamus. Although the neurohypophysis and AVP production remain normal, damage to these osmoreceptors leads to reduced stimulation of AVP secretion. This results in symptoms related to deficient AVP secretion without causing polydipsia, as the damaged osmoreceptors are also responsible for triggering thirst in response to increased plasma osmolality. This is called Adipsic AVP-D (adipsic diabetes insipidus).

causes

ACQUIRED

- Neurosurgery or trauma
- Malignancy
- Drugs (ipilimumab) discontinuation of vasopressin infused to treat hypotension
- Infections (rare)
- Idiopathic

GENETIC

- Familial AVP-D
- Wolfram syndrome (AVP-D, diabetes mellitus, opticatrophy, and deafness, with cognitive and psychiatric issues)
- PCSK1 gene deficiency
- Congenital hypopituitarism

NEPHROGENIC DIABETES INSIPIDUS (ARGININE VASOPRESSIN RESISTANCE)

- In nephrogenic diabetes insipidus (AVP-R), your body makes enough vasopressin but your kidneys don’t respond to the hormone as they should.

CAUSES

1.Genetic :
mutation in ADH receptor
or in Aquaporin

2. Acquired :
- Drugs (lithium , demeclocycline)
- Hypercalcemia , Hypokalemia
-Secondary to other diseases (sjogren's syndrome, polycystic kidney disease, sickle cell anemia)

GESTATIONAL DIABETES INSIPIDUS

This is a rare, temporary condition that can develop during the end of the second trimester or during the third trimester of pregnancy.

Gestational diabetes insipidus happens when the placental trophoblasts make too much of an enzyme called VASOPRESSINASE that breaks down ADH.

Its activity is proportional to the placental weight, explaining the higher vasopressinase activity in third trimester or in multiple pregnancies.

Dipsogenic Diabetis Insipidus

People who have this disorder constantly feel thirsty and drink lots of fluids. It can be caused by damage to the thirst-regulating mechanism in the hypothalamus. It differs from other types of diabetes insipidus because it does not affect how your body handles ADH.

CAUSES : hypothalamus damage related to:

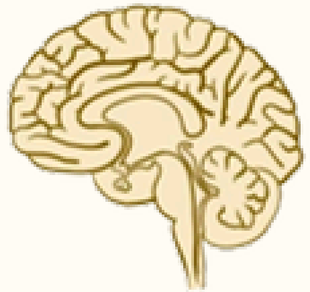
surgery, infection, inflammation, brain injury or tumor

Diabetes Insipidus

(Excessive **WATER** Loss Through **URINE**)

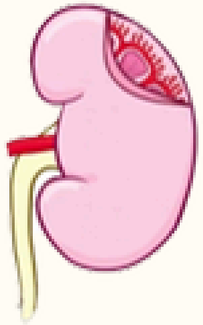
Central

ADH is Not Being Produced or Released



Nephrogenic

Kidneys Do Not Respond to **ADH**



Gestational

Caused By Vasopressinase

Dipsogenic

Excessive **WATER** Intake

SUMMARY

	CENTRAL	NEPHROGENIC	DIPSOGENIC
AVP	Decreased	Normal or increased	Normal or decreased
Mechanism	AVP deficiency	AVP resistance	Compulsive water intake
Etiology	Primary: idiopathic Secondary: brain lesionsor injury (e.g., tumors, hypoxic injury, surgery)	AVP receptor mutation Medications (lithium, demeclocycline) Electrolyte disturbances (hypercalcemia, hypokalemia) Renal disease Pregnancy	Psychiatric diseases (schizophrenia, obsessive-compulsive disorder) Lesions in the hypothalamic thirst center

Clinical manifestations

Clinical manifestations

Polyuria (excessive urine output, typically >40-50 mL/kg/day)

NOCTURIA (NEED TO URINATE AT NIGHT)

POLYDIPSIA (EXCESSIVE THIRST) DUE TO INITIAL ELEVATION IN SERUM SODIUM AND OSMOLALITY.

In cases of low water intake

Severe Dehydration
(Altered Mental Status, Lethargy, Seizures, Coma) and Hypotension

Clinical manifestations

- SERUM SODIUM OFTEN IN THE HIGH NORMAL RANGE IN UNTREATED PATIENTS
- MODERATE TO SEVERE HYPERNATREMIA CAN DEVELOP IF THIRST IS IMPAIRED OR THERE'S NO ACCESS TO WATER
- NEUROLOGIC SYMPTOMS RELATED TO THE UNDERLYING CAUSE (E.G. DIPLOPIA, HEADACHE)
- PSYCHOLOGICAL SYMPTOMS SUCH AS:

- Increased anxiety - Social isolation - Generally decreased quality of life

DM vs DI

Feature	Diabetes Mellitus	Diabetes Insipidus
Hormone involved	Insulin	ADH (vasopressin)
Primary Issue	High blood glucose	Excessive urination, dilute urine
Common Symptoms	Polyuria, polydipsia, hyperglycemia	Excessive urination, dilute urine
Urine Osmolality	High (in uncontrolled cases)	Low
Blood Sodium	Low (in uncontrolled cases)	Typically normal or high
Treatment	Insulin or hypoglycemics	Desmopressin for central DI, hydration

Diagnosis

Diagnosing and Evaluating of (AVP-D/R)

Overview of Diagnostic Steps

STEP 1: CONFIRM POLYURIA

- Measure urine output to confirm polyuria (typically >40-50 mL/kg/day).
- Conduct a 24-hour urine collection to quantify excessive urine production, as seen in both

STEP 2: DIFFERENTIATE WATER DIURESIS FROM SOLUTE DIURESIS

Determine if polyuria is due to water diuresis (less than 300mOsm/kg, typical in diabetes insipidus) or solute diuresis (more than 600mOsm/kg, typical in DM or medication-induced).

STEP 3: CONFIRM AVP-D OR AVP-R DIAGNOSIS

1) Water deprivation test: A test to assess the kidney's ability to conserve water by restricting fluid intake.
2) Desmopressin challenge: A test to evaluate the body's response to synthetic vasopressin (desmopressin) to differentiate between central and nephrogenic diabetes insipidus .

Diagnosing and Evaluating of (AVP-D/R)

Water deprivation test

No water 2-3 hours prior to test

- Measure urine volume & osmolality every hour
- Measure serum sodium & osmolality every 2 hours

Urine osmolality >600 mOsm/kg

YES! → Primary polydipsia

NO!

- Urine osmolality stable on 2-3 consecutive hourly measurements
- Plasma osmolality >295 mOsm/kg or plasma sodium >145 mEq/L

YES! →

- Administer desmopressin
- Monitor urine osmolality & volume every 30 minutes for 2 hours

NO!

Continue testing until above endpoints are reached

- Central DI: ⬆ urine osmolality 50%-100%
- Nephrogenic DI: Small or no ⬆ in urine osmolality

Diagnosing and Evaluating of (AVP-D/R)

OVERVIEW OF DIAGNOSTIC STEPS

Step 4: Determine Etiology

- For Post-Surgical or Trauma Patients: In AVP-D, deficiency is often transient following neurosurgery or head trauma.
- MRI Imaging:

— For AVP-D: Perform brain MRI to examine the suprasellar region, pituitary stalk, and pituitary gland, especially for structural abnormalities or tumors.

In some patients, MRI will identify the cause of AVP-D, such as a malignancy or infarction.

*It is important to note that primary tumors of the pituitary gland are slow-growing and almost never cause AVP-D; therefore, if such a tumor is diagnosed, alternative etiologies of the AVP-D should be investigated.

— For AVP-R: Kidney ultrasound or MRI may be used if there are concerns about structural renal abnormalities.

- Identify Underlying Causes:
- For AVP-R: Check for factors like lithium(Li) use, hypercalcemia(Ca), or hypokalemia(K).

Diagnosing and Evaluating of (AVP-D/R)

OVERVIEW OF DIAGNOSTIC STEPS

Step 5: Evaluate Risk of Complications and Monitor High-Risk Groups

- Both AVP-D and AVP-R patients should be monitored for Dehydration and Hypernatremia, especially if they have impaired thirst.
- High-risk populations include infants, young children, neurologically impaired adults, and postoperative patients.

Step 7:Consider Genetic Testing

- For patients with family history suggestive of DI

Step 6: Follow-Up and Long-Term Monitoring

- For AVP-D: If initial tests are negative, repeat MRI in 3-6
  months and then yearly for up to 5 years;
  assess anterior pituitary function yearly.
- For AVP-R: Routine follow-up to monitor urine output,
  electrolyte balance, and associated conditions
  (e.g., lithium therapy) is advised.

Management

Management

THE FIRST CONCERN IS ADEQUATE HYDRATION AND REPLACEMENT OF WATER DEFICIT

Management

- In most individuals who have normal thirst mechanism, it can guide the intake of oral fluids. However, in individuals with adipsic DI who have impaired thirst, a daily fluid intake should be fixed at which euvolemia and eunatremia are maintained.
- In unconscious patients, water deficit can be corrected with plain water administered through Ryle's tube and with intravenous hypotonic fluids (5% dextrose or 0.45 saline).
  Isotonic fluid (0.9 saline) should be avoided as it can worsen hypernatremia.

Management

- IF THE SERUM NA+ IS ALREADY HIGH (>145MMOL/L)
  DON'T RESTRICT THE WATER (TO AVOID HYPERNATREMIA).
  MEASURE PLASMA AND URINE OSMOLALITY &
  SKIP TO DEMOPRESSIN ADMINISTRATION .

- IF THE SERUM NA+ IS IN THE NORMAL LEVEL
  FIRST : RESTRICT THE WATER/FLUID INTAKE
  THEN MEASURE PLASMA OSMOLALITY
  URINE OSMOLALITY & SERUM NA+ EVERY 2 HOURS .

TREATMENT

Treatment

CENTRAL DI

- DESMOPRESSIN (SYNTHETIC ADH ANALOG)

  IS THE PRIMARY THERAPY FOR DI. IT HAS THE ANTI-DIURITIC EFFECT OF THE ADH WITHOUT THE VASOCONSTRICTIVE EFFECT .

  IT CAN BE GIVEN INTRANASALLY (MOST POTENT) , ORALLY, OR BY INJECTION.

  START WITH A LOW DOSE TO AVOIDE OVERCORRECTION .

- TREAT THE UNDERLYING CAUSE.

Treatment

NEPHROGENIC DI

- Thiazide Diuretics

  The induction of mild volume depletion with a low-sodium diet plus the thiazide diuretic (such as hydrochlorothiazide)is a first-line therapy in AVP-R .
  Thiazide diuretics inhibit the sodium-chloride co-transporter in the distal convoluted tubule. By blocking sodium reabsorption, they cause increased sodium (and accompanying water) to remain in the urine.
  The decrease in sodium reabsorption results in a reduction of extracellular fluid volume. This triggers compensatory water reabsorption in the proximal tubule despite the ineffective action of ADH.

Treatment

NEPHROGENIC DI

- NSAIDs like IBUPROFEN or INDOMETHACIN.
  They increase urinary concentrating ability by inhibiting the renal synthesis of prostaglandins, which are ADH antagonists and increases the antidiuretic effect of a submaximal dose of ADH.
  NOTE : in paitents with renal disease , NSAIDs must be used with caution because of the potential nephrotoxic effects.
- Amiloride may be particularly beneficial in patients with reversible lithium nephrotoxicity.

Treatment

GESTATIONAL DI

- DESMOPRESSIN

DIPSOGENIC DI

- BEHAVIORAL THERAPY

references

- UpToDate® :

https://www.uptodate.com/contents/arginine-vasopressin-deficiency-central-diabetes-insipidus-treatment?search=AVP%20D&source=search_result&selectedTitle=1%7E84&usage_type=default&display_rank=1#H27520276
https://www.uptodate.com/contents/arginine-vasopressin-deficiency-central-diabetes-insipidus-etiology-clinical-manifestations-and-postdiagnostic-evaluation?search=AVP+D&source=search_result&selectedTitle=2%7E84&usage_type=default&display_rank=2
https://www.uptodate.com/contents/arginine-vasopressin-resistance-nephrogenic-diabetes-insipidus-etiology-clinical-manifestations-and-postdiagnostic-evaluation?search=AVP+R&source=search_result&selectedTitle=1%7E79&usage_type=default&display_rank=1
https://www.uptodate.com/contents/arginine-vasopressin-resistance-nephrogenic-diabetes-insipidus-treatment?search=AVP+R&source=search_result&selectedTitle=2%7E79&usage_type=default&display_rank=2

- AMBOSS :

https://next.amboss.com/us/article/_T05t2

- OTHERS :

https://www.ncbi.nlm.nih.gov/books/NBK537591/
https://pmc.ncbi.nlm.nih.gov/articles/PMC4626653/
HTTPS://PUBMED.NCBI.NLM.NIH.GOV/30252325/

Thank You

"كل ليلة ديربي هي أسوأ كوابيسك"